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Impact of adolescent and advanced maternal age on maternal and neonatal outcomes in the Born in Bradford Cohort

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ABSTRACT

Objectives: Explore associations between maternal and neonatal outcomes and maternal age, with particular reference to adolescents and older women.

Design: Population based cohort study

Setting: Maternity department of a large hospital in northern England

Participants: Women delivering a singleton at Bradford Royal Infirmary between March 2007 and December 2010 (N=11,250) were divided into three age groups for primary analysis (≤19 years, 20-34 years and 35≥ years) and a further two groups for sub-group analysis (≤16 years and ≥40 years). Women aged 20-34 years were used as the reference group.

Primary outcome measures: Maternal and neonatal outcomes

Results: The odds of extremely low birthweight (<1000g) were significantly higher in the adolescent group (≤19 years) compared to the reference group (aOR 3.71, CI 1.05 to 13.13). Sub-group analysis also found that the youngest adolescents (≤16 years) had increased odds of developing pre-eclampsia (aOR 3.81, CI 1.30 to 11.13) compared to the reference group.

Women aged 35 and over were at increased odds of gestational diabetes (aOR 2.09, CI 1.72 to 2.53) and caesarean delivery (aOR 1.94, CI 1.38 to 2.24); the reverse was true for adolescent mothers. Sub-group analysis of women aged ≥40 years showed an increased risk of stillbirth (aOR 3.82, CI 1.10 to 13.30), low birthweight (aOR 2.21, CI 1.37 to 3.55), premature delivery (aOR 2.05, CI 1.22 to 3.44) and APGAR score below 7 at 5 minutes (aOR 2.69, CI 1.42 to 5.12).

Conclusions: This study identifies important differences in maternal and neonatal outcomes between women by age group. These findings could help in identifying at risk groups for additional support and tailored interventions to minimise the risk of adverse outcomes for these vulnerable groups. Further work is needed to identify the causal mechanisms linking age with outcomes, particularly in adolescent women where significant gaps in the literature exist.

Key words: Adolescents; Adults; Women; Pregnancy; Outcomes; Born in Bradford

STRENGTHS AND LIMITATIONS OF THIS STUDY

- A particular strength of this work is that it utilises well-established, ethnically diverse, UK based cohort data in a way which is unique to this study.

- A further strength is in the large number of participants available for analysis which enables robust conclusions to be drawn.
- Despite the large number of participants however, this study is limited by small numbers of occurrences of some rare outcomes, particularly in sub-group analyses.
- It should also be considered that the generalisability of this study to contexts which are very different in terms of socioeconomic and demographic characteristics is limited.

INTRODUCTION

The impact of maternal age on obstetric and neonatal outcomes has been studied in various parts of the world and with variable results, particularly with reference to the youngest and the oldest mothers. Pregnancy during adolescence is often associated with less favourable outcomes for both mother and child. Childbearing in adolescence is associated with social problems such as isolation, poverty, low levels of education and unemployment.[1] There is also evidence to suggest that health outcomes may be less favourable for younger mothers. A number of studies have suggested that babies born to adolescent mothers are at higher risk of premature birth and low birthweight [2-3] and that stillbirth and neonatal mortality may be more prevalent in this group.[4] Adolescents have however been consistently shown to have lower rates of caesarean and instrumental delivery [5] and therefore are at lower risk of complications associated with assisted births. It is not currently clear from the available literature however to what extent differences in birth outcomes between adolescent and adult mothers are predicted by age alone.

Advanced maternal age has shown to be an important independent risk factor of poor outcomes. The North Western Perinatal Survey, a large cohort study based at the University of Manchester, UK, found that women aged over 40 were at increased risk of poor outcomes compared to those aged 20-29 including stillbirth, pre-term delivery, macrosomia and caesarean section [6] after adjustment for confounding variables (parity, ethnicity, social deprivation score and body mass index). This suggests that age is an important variable to consider for maternal and infant health.

A number of studies have suggested that neonatal outcomes are less favourable among babies born to adolescent mothers. A systematic review [7] aiming to assess the relationship between early first childbirth and increased risk of poor pregnancy outcomes found that there was considerable evidence to suggest that very young maternal age (<15 years or less than 2 years after menarche) had a negative effect on both maternal and foetal growth and infant survival. It is suggested that young women who are still themselves growing may compete with the foetus for nutrients, which may in turn impair foetal growth and result in low birth weight babies or babies who are small for their gestational age. The review also found a moderately increased risk of anaemia, premature birth and neonatal mortality associated with young maternal age.

It is possible however that maternal age is a less important factor for younger women in itself, but rather is associated with other demographic and behavioural characteristics which impact upon birth outcomes. Lifestyle and socio-demographic factors such as smoking,[8] alcohol use [9] and deprivation [10] have all been shown to contribute to less favourable birth outcomes. It is also established that adolescent mothers in high income countries are at higher risk of exhibiting these characteristics. [11]

The Born in Bradford study is a cohort of approximately 13,500 children born at Bradford Royal Infirmary between March 2007 and December 2010. The cohort reflects the diversity of the population in Bradford and as such is a largely bi-ethnic sample with high levels of socio-economic deprivation, which presents a unique opportunity to explore any differences in birth outcomes between adolescent and adult women and the factors which contribute to these differences. A detailed profile of the cohort has been previously published. [12]

Some work has already been carried out looking at maternal and neonatal outcomes in the Born in Bradford cohort, particularly with reference to maternal ethnicity. A study looking at differences in socioeconomic status, lifestyle and health-related pregnancy characteristics between Pakistani and White British women [13] found that White British women were more likely to smoke and have a higher body mass index (BMI) compared to Pakistani women, however Pakistani women were more likely to have gestational diabetes. A further study found that infants born to Pakistani women were lighter at birth compared to those born to White British mothers.[14]

While these studies have shown some interesting associations between maternal and neonatal outcomes and maternal ethnicity, the impact of maternal age on outcomes is yet to be explored in this cohort. The size and diversity of this cohort allow for detailed analysis to be carried out and factors known to impact on maternal and neonatal outcomes to be controlled for, making this study unique in a UK context. For these reasons the primary aim of this investigation is to explore the relationship between maternal and neonatal outcomes and maternal age in the Born in Bradford cohort.

METHODS

This study utilises the Born in Bradford cohort and analyses maternal and neonatal outcomes of all women delivering singletons who took part in the study. Data from the Born in Bradford baseline questionnaire provides information on maternal characteristics and is linked to hospital maternity records providing data on maternal and neonatal outcomes. The Born in Bradford study is a prospective cohort study for which participants were recruited during pregnancy. All women booked for delivery at Bradford Royal Infirmary are offered an oral glucose tolerance test (OGTT) at 26-28 weeks gestation. Women were invited to participate in the Born in Bradford study when attending this appointment. Informed consent was obtained and women were asked to complete a baseline questionnaire. Recruitment took place between March 2007 and December 2010 and over 80% of women eligible in this period agreed to take part.[12] Data relating to 11,250 pregnancies was available for this analysis. Ethical approval for the study was granted by Bradford Research Ethics Committee (ref no. 07/H1302/112).

Outcome variables

The maternal outcome variables included in this analysis were diagnosis of pre-eclampsia (diagnosis in this cohort was made when proteinuria is >0.3mgs and blood pressure is ≥140/90 on more than one occasion.), diagnosis of gestational diabetes (defined as a 2 hour post glucose load plasma glucose level of 7.8 mmol/ or a fasting plasma glucose level of 6.1mmol/l),[13] mode of birth (normal vaginal, instrumental (including both forceps and ventouse deliveries) or caesarean section). The neonatal outcome variables studied were low birthweight (below 2500g), very low birthweight (below 1500g), extremely low birthweight (below 1000g), macrosomia (birthweight

over 4000g), small for gestational age (birthweight lower than the 10th percentile for the sample), large for gestational age (birthweight higher than the 90th percentile for the sample), premature birth (<37 completed weeks gestation), very premature birth (<32 completed weeks gestation), extremely premature birth (<28 completed weeks gestation), outcome of birth (live birth or stillbirth) and APGAR score at 1 and 5 minutes (analysed as two groups, <7 and 7-10).

Statistical Analysis

The study population was categorised into three groups according to maternal age; ≤19, 20-34 and 35≥ years. In the analyses of outcomes the maternal age group 20-34 was selected as the reference group as this group is the least likely to suffer age related complications as discussed in the introduction.

Characteristics of the sample were described; presenting categorical variables as percentages and continuous variables as means and standard deviations. This analysis was carried out both for demographic characteristics and for maternal and neonatal outcome variables. Differences between maternal age groups were explored using Chi-Square for categorical data and one-way ANOVA for continuous data.

Logistic regression analyses were used to explore the relationships between maternal age group and the outcome variables. Multivariate logistic regression models were then used to adjust these comparisons for confounding variables. Crude and adjusted odds ratios (OR and aOR) are therefore presented with 95% confidence intervals. Continuous variables included in the adjusted analysis as confounders were maternal body mass index (BMI) at the booking appointment, number of weeks gestation at the booking appointment and index of multiple

deprivation (IMD) score. Categorical cofounders included were maternal ethnicity (white British, Pakistani or any other ethnicity), smoking at any time during pregnancy (yes or no), and parity (0, 1, 2 or 3 or more). Where data were missing for any of the variables included in the logistic regression model the case was excluded from the analysis. There was significant variation in the number of participants with missing data for individual variables and missing data for alcohol use variables was particularly prevalent. For this reason alcohol use was not adjusted for in the model in order to maximise the number of cases available for analysis.

In the multivariate logistic regression model for this study there is no clear logical or theoretical basis for assuming any variable to be prior to any other, either in terms of its relevance to the research goal of explaining phenomena, or in terms of a hypothetical causal structure of the data. For this reason a simultaneous model of including independent variables in the multivariate logistic regression model was considered to be most appropriate.

Further sub-group analysis was also undertaken to explore any further associations at the extreme ends of the age spectrum. Multivariate logistic regression models were developed to examine the maternal and neonatal outcomes across five categories of maternal age; ≤16, 17-19, 20-34, 35-39 and 40≥ and reported in the same way as the main analysis.

Statistical analysis was undertaken using SPSS 24.

RESULTS

Characteristics of the sample

Data were available for 11,250 pregnancies for this analysis; characteristics of the participants included in the study are shown in table 1. The majority of participants in the cohort were aged 20-34 (81%) with 12.7% aged 35 or over and only 5.7% aged 19 or under. The cohort overall is made up of 45% Pakistani women, 39.5% white British woman and 15.5% women of other ethnicities; this distribution of ethnic groups was roughly consistent across the age groups with the exception of the adolescent group which was significantly different. Among women aged 19 and under only 17.2% were of Pakistani ethnicity and 69.2% were white British, the proportion belonging to other ethnic groups was similar to other age groups. There were other significant variations in the characteristics of the sample by maternal age. Women in the adolescent age group were more likely to not be married or living with a partner, to be expecting their first child and to have completed lower levels of education compared to older women. Women in the adolescent age groups were also more likely to have smoked or used recreational drugs during pregnancy, however there was no difference in reported alcohol use in the first trimester between age groups and adolescents were less likely to have used alcohol since the fourth month of their pregnancy compared to older women. Women in the oldest age category were most likely to be overweight or obese while adolescent women were found to have higher prevalence of underweight. Older women were also more likely to have taken nutritional supplements in the four weeks before questionnaire completion compared to younger women. Analysis of continuous variables showed that IMD score decreased as maternal age increased suggesting adolescent women lived in areas of higher deprivation. Adolescent women also booked with a midwife for antenatal care later than older women; there was a mean difference of 2 weeks between the youngest and oldest age groups.

Table 1 Characteristics of the sample by maternal age

	≤19		20-34		35≥		Total		Missing	
	N	%	N	%	N	%	N	%	N	p=
Whole Cohort	641	5.7	9114	81.0	1427	12.7	11250	100.0		<0.001
Ethnicity									25	
Pakistani	122	17.2	4322	47.5	609	42.8	5053	45.0		<0.001
White British	492	69.4	3365	37.0	574	40.3	4431	39.5		
Any other ethnicity	95	13.4	1406	15.5	240	16.9	1741	15.5		
Marital Status									25	
Married	103	14.5	6194	68.1	1082	76.0	7379	65.7		<0.001
Not married - living with partner	167	23.6	1630	17.9	206	14.5	2003	17.8		
Single	439	61.9	1269	14.0	135	9.5	1843	16.4		
Parents related other than by marriage									12	
Yes	85	12.0	2885	31.7	395	27.7	3365	29.9		<0.001
No	624	88.0	6219	68.3	1030	72.3	7873	70.1		
Parity									**0**	
0	640	90.3	3951	43.4	303	21.2	4894	43.5		<0.001
1	64	9.0	2712	29.8	340	23.8	3116	27.7		
2	5	0.7	1481	16.2	292	20.5	1778	15.8		
3 or more	0	0.0	970	10.6	492	34.5	1462	13.0		
Highest level of education									30	
Less than 5 GCSEs grade A-C or equivalent	270	38.1	1768	19.4	380	26.7	2418	21.6		<0.001
5 GCSEs grade A-C or equivalent	322	45.5	2832	31.2	294	20.7	3448	30.7		
A-levels or higher	62	8.8	3842	42.3	598	42.1	4502	40.1		
Other/unknown	54	7.6	648	7.1	150	10.5	852	7.6		
Smoked during pregnancy									**21**	
Yes	377	53.2	1376	15.1	140	9.8	1848	16.5		<0.001

No	332	46.8	7720	84.9	1284	90.2	9381	83.5		
Drunk alcohol in the first three months of pregnancy									7801	
Yes	193	55.6	1279	48.7	247	52.0	1719	49.8		0.089
No	153	44.1	1342	51.1	228	48.0	1723	50.0		
Don't remember			6	0.2	0	0.0	7	0.2		
Drunk alcohol since the fourth month of pregnancy									7839	
Yes	96	27.8	981	37.7	215	46.4	1292	37.9		<0.001
No	248	71.9	1620	62.2	248	53.6	2116	62.0		
Don't remember			2	0.1	0	0.0	3	0.1		
Used recreational drugs during pregnancy									1631	
Yes	30	5.1	87	1.1	8	0.7	125	1.3		<0.001
No	564	94.9	7721	98.9	1209	99.3	9494	98.7		
Used any vitamins or iron supplements in the last 4 weeks									39	
Yes	170	24.0	3600	39.6	708	49.8	4478	39.9		<0.001
No	538	76.0	5481	60.4	714	50.2	6733	60.1		
BMI Category									1018	
Underweight (Below 18.5)	62	9.5	368	4.4	13	1.0	450	4.3		<0.001
Healthy weight (18.5 - 24.9)	395	60.6	3840	46.4	476	36.6	4643	45.4		
Overweight (25 - 29.9)	132	20.2	2340	28.3	476	36.6	2948	28.8		
Obese (30 or higher)	63	9.7	1732	20.9	403	31.0	2198	21.5		
	N	**Mean (SD)**	**N**	**Mean (SD)**	**N**	**Mean (SD)**	**N**	**Mean (SD)**		**p=**
BMI at booking appointment	660	23.5 (4.8)	8396	25.9 (5.7)	1312	28.1 (5.8)	10368	26.0 (5.7)	882	<0.001
IMD Score	709	44.8 (17.8)	9111	42.8 (17.7)	1427	38.0 (18.4)	11247	42.3 (17.8)	3	<0.001
Number of weeks gestation at booking appointment	656	13.2 (3.7)	8465	12.4 (3.0)	1317	12.6 (2.8)	10438	12.5 (3.1)	812	<0.001

Descriptive analysis relating to maternal and neonatal outcomes is shown in table 2. This analysis suggests that there are several outcome variables which show significant variation by maternal age group. Among the neonatal outcomes the results show babies born to adolescent women were significantly more likely to have very or extremely low birthweights or to be born very or extremely prematurely. Older women were shown to be more likely to deliver babies who were for macrosomic or large for their gestational age. Among the maternal outcomes higher rates of both gestational diabetes and caesarean delivery were associated with older maternal age.

Table 2 Descriptive analysis of maternal and neonatal outcomes by maternal age

	≤19 (n=641)		20-34 (n=9114)		35≥ (n=1427)		Total (n=11250)		Missing	
	N	%	N	%	N	%	N	%	N	p=
Neonatal Outcomes										
Low birthweight (<2500g)	64	9.0	666	7.3	107	7.5	837	7.4	1	0.243
Very low birthweight (<1500g)	11	1.6	70	0.8	7	0.5	88	0.8	0	0.030
Extremely low birthweight (<1000g)	7	1.0	20	0.2	5	0.4	32	0.3	0	0.001
Macrosomia (Birthweight >4000g)	42	5.9	686	7.5	129	9.0	857	7.6	1	0.029
Small for gestational age	87	12.5	1066	11.9	150	10.6	1303	11.8	165	0.328
Large for gestational age	68	9.6	1257	13.8	262	18.4	1587	14.1	0	<0.001
Premature birth (<37 weeks)	49	6.9	491	5.4	84	5.9	624	5.5	0	0.194
Very premature birth (<32 weeks)	13	1.8	78	0.9	11	0.8	102	0.9	0	0.026
Extremely premature birth (<28 weeks)	4	0.6	13	0.1	4	0.3	21	0.2	0	0.030
Stillborn	7	1.0	48	0.5	5	0.4	60	0.5	0	0.160
APGAR score <7 at 1 minute	84	11.8	877	9.6	138	9.7	1099	9.8	0	0.156
APGAR score <7 at 5 minutes	27	3.8	259	2.8	52	3.6	338	3.0	0	0.111
Maternal Outcomes										
Pre-eclampsia	19	2.7	215	2.4	44	3.1	278	2.5	0	0.244
Gestational Diabetes	14	2.0	658	7.2	232	16.3	904	8.0	0	<0.001
Caesarean Delivery	102	14.4	1911	21.0	459	32.2	2472	22.0	0	<0.001
Instrumental birth¥	79	13.0	890	12.4	105	10.8	1074	12.2	7	0.331

¥ Vaginal deliveries only, included both forceps and ventouse deliveries

Logistic Regression Analysis

The crude and adjusted odds ratios for maternal and neonatal outcomes by maternal age group are shown in table 3.

Maternal and Neonatal outcomes of adolescents

Women in this age group were found to have a significantly higher odds of delivering extremely low birthweight babies (<1000g) compared to the reference group (aOR 3.71, CI 1.05 to 13.13). Adolescent pregnant women experienced lower odds of being diagnosed with gestational diabetes than the reference group (aOR 0.33, CI 0.17 to 0.64). The odds of women in this age group delivering by caesarean section were decreased (aOR 0.61, CI 0.48 to 0.78, as were the odds of having an instrumental delivery (aOR 0.57, CI 0.43 to 0.75) compared to the reference group.

Maternal and Neonatal outcomes of Women aged 35 and over

Women in the older age category were shown to be at increased risk of being diagnosed with gestational diabetes (aOR 2.09, CI 1.72 to 2.53) compared to women in the reference group. For older women the odds of both delivering by caesarean section (aOR 1.94, CI 1.38 to 2.24) and of having an instrumental delivery (aOR 1.63, CI 1.26 to 2.11) increased compared to women aged 20-34.

No significant differences were observed in neonatal outcomes between women aged 35 and over and the reference group.

Table 3 Neonatal and maternal outcomes by maternal age group

	Crude OR (95% CI)	aOR (95% CI)*	Crude OR (95% CI)	aOR (95% CI)*
	≤19 Years (n=641)		35≥ Years (n=1427)	
Neonatal Outcomes				
Low birthweight (<2500g)	1.26 (0.96 to 1.65)	1.00 (0.73 to 1.36)	1.03 (0.83 to 1.27)	1.19 (0.92 to 1.55)
Very low birthweight (<1500g)	2.04 (1.07 to 3.86)	1.30 (0.58 to 2.93)	0.80 (0.24 to 2.63)	0.71 (0.27 to 1.82)
Extremely low birthweight (<1000g)	4.53 (1.91 to 10.76)	3.71 (1.05 to 13.13)	2.98 (0.58 to 15.38)	1.18 (0.31 to 4.47)
Macrosomia (Birthweight >4000g)	0.77 (0.56 to 1.07)	0.97 (0.66 to 1.41)	1.22 (1.00 to 1.49)	0.93 (0.74 to 1.16)
Small for gestational age	1.06 (0.84 to 1.34)	0.89 (0.68 to 1.16)	0.88 (0.74 to 1.06)	1.20 (0.97 to 1.49)
Large for gestational age	0.66 (0.51 to 0.86)	0.83 (0.61 to 1.13)	1.41 (1.21 to 1.63)	1.09 (0.92 to 1.29)
Premature delivery (<37 weeks)	1.30 (0.96 to 1.77)	0.96 (0.67 to 1.37)	1.10 (0.87 to 1.39)	1.14 (0.86 to 1.52)
Very premature delivery (<32 weeks)	2.16 (1.20 to 3.91)	1.81 (0.85 to 3.83)	1.04 (0.44 to 2.45)	0.67 (0.28 to 1.60)
Extremely premature delivery (<28 weeks)	3.97 (1.29 to 12.21)	3.10 (0.67 to 14.40)	2.48 (0.50 to 12.32)	1.22 (0.24 to 6.18)
Stillborn	1.88 (0.85 to 4.18)	1.09 (0.31 to 3.81)	0.66 (0.26 to 1.67)	1.01 (0.37 to 2.71)
APGAR score <7 at 1 minute	1.26 (1.00 to 1.60)	1.02 (0.77 to 1.34)	1.01 (0.83 to 1.22)	0.98 (0.78 to 1.23)
APGAR score <7 at 5 minutes	1.35 (0.90 to 2.03)	0.82 (0.50 to 1.37)	1.29 (0.96 to 1.75)	1.25 (0.85 to 1.84)
Maternal Outcomes				
Pre-eclampsia	1.14 (0.71 to 1.83)	1.29 (0.77 to 2.18)	1.32 (0.95 to 1.83)	1.40 (0.96 to 2.03)
Gestational Diabetes	0.26 (0.15 to 0.44)	0.33 (0.17 to 0.64)	2.50 (2.12 to 2.93)	2.09 (1.72 to 2.53)
Caesarean Delivery	0.63 (0.51 to 0.79)	0.61 (0.48 to 0.78)	1.79 (1.58 to 2.02)	1.94 (1.38 to 2.24)
Instrumental birth¥	1.06 (0.83 to 1.36)	0.57 (0.43 to 0.75)	0.86 (0.70 to 1.07)	1.63 (1.26 to 2.11)

Reference group: Maternal age 20-34 years, *Adjusted for maternal BMI at booking, number of weeks gestation at booking, IMD score, ethnicity, smoking during pregnancy, and parity

¥ Vaginal deliveries only, included both forceps and ventouse deliveries

Sub-group analysis

For some outcomes the number of events occurring in the sub groups, particularly the group aged ≤16, was either very small or no events took place. This resulted in either the regression model failing to produce a valid result or the aOR being subject to extremely wide confidence intervals. The results presented do however provide a useful indication of the outcomes which may be important for further investigation. Results of the sub-group analysis are shown in table 4.

Women aged 16 or under

The youngest women included in the analysis were found to have significantly higher odds of developing pre-eclampsia compared to the reference group (aOR 3.81, CI 1.30 to 11.13). There were no other significant differences observed in this group.

Women aged 40 or over

In addition to the outcomes identified in the analysis of women aged 35 and over, women aged 40 or more were also at increased risk of a number of adverse neonatal outcomes compared to the reference group. Babies born to women in the oldest group were at increased odds of low birth weight (aOR 2.21, CI 1.37 to 3.55) and premature birth (<37 completed weeks gestation) (aOR 2.05, CI 1.22 to 3.44) compared to the reference group. The analysis for older mothers also showed an increase in the odds of having an APGAR score below 7 at 5 minutes after birth (aOR 2.69, CI 1.42 to 5.12) and an increase in the odds of stillbirth (aOR 3.82, CI 1.10 to 13.30) compared to the reference group.

Table 4 Sub-group analysis of neonatal and maternal outcomes

	Crude OR (95% CI)	aOR (95% CI)*	Crude OR (95% CI)	aOR (95% CI)*
	≤16 Years (n=57)		40≥ Years (n=199)	
Neonatal Outcomes				
Low birthweight (<2500g)	1.01 (0.40 to 2.51)	0.71 (0.25 to 2.02)	1.69 (1.13 to 2.53)	2.21 (1.37 to 3.55)
Very low birthweight (<1500g)	8.54 (1.99 to 36.67)	4.50 (0.52 to 39.14)	1.10 (0.27 to 4.49)	1.83 (0.43 to 7.82)
Extremely low birthweight (<1000g)	23.6 (2.72 to 205.00)	**	3.85 (0.90 to 16.58)	4.68 (0.96 to 22.81)
Macrosomia (Birthweight >4000g)	0.57 (0.18 to 1.81)	0.63 (0.15 to 2.62)	1.31 (0.85 to 2.03)	0.85 (0.51 to 1.41)
Small for gestational age	0.73 (0.32 to 1.69)	0.63 (0.25 to 1.61)	0.92 (0.61 to 1.38)	1.43 (0.90 to 2.27)
Large for gestational age	0.83 (0.40 to 1.75)	1.34 (0.60 to 3.01)	1.66 (1.21 to 2.28)	1.16 (0.81 to 1.67)
Premature delivery (<37 weeks)	1.39 (0.56 to 3.48)	0.93 (0.33 to 2.63)	1.97 (1.28 to 3.03)	2.05 (1.22 to 3.44)
Very premature delivery (<32 weeks)	2.73 (0.37 to 20.14)	**	0.98 (0.24 to 4.02)	1.41 (0.33 to 5.98)
Extremely premature delivery (<28 weeks)	19.66 (2.33 to 165.79)	**	2.95 (0.39 to 22.67)	3.90 (0.45 to 33.90)
Stillborn	**	**	2.41 (0.75 to 7.80)	3.82 (1.10 to 13.30)
APGAR score <7 at 1 minute	1.43 (0.71 to 2.90)	1.43 (0.69 to 2.97)	1.41 (0.96 to 2.07)	1.48 (0.95 to 2.30)
APGAR score <7 at 5 minutes	1.04 (0.25 to 4.25)	0.84 (0.20 to 3.64)	2.46 (1.46 to 4.15)	2.69 (1.42 to 5.12)
Maternal Outcomes				
Pre-eclampsia	2.59 (0.93 to 7.17)	3.81 (1.30 to 11.13)	1.63 (0.82 to 3.21)	1.84 (0.89 to 3.78)
Gestational Diabetes	**	**	2.68 (1.89 to 3.78)	1.95 (1.29 to 2.94)
Caesarean Delivery	0.37 (0.16 to 0.84)	0.36 (0.14 to 0.91)	2.46 (1.89 to 3.21)	2.53 (1.86 to 3.44)
Instrumental birth¥	1.88 (1.02 to 3.48)	1.13 (0.58 to 2.20)	0.64 (0.36 to 1.17)	1.60 (0.82 to 3.15)

Reference group: Maternal age 20-34 years, *Adjusted for maternal BMI at booking, number of weeks gestation at booking, IMD score, ethnicity, smoking during pregnancy, and parity, **No valid result available due to small numbers

¥ Vaginal deliveries only, included both forceps and ventouse deliveries

DISCUSSION

Analysis of maternal and neonatal outcomes in the Born in Bradford cohort in this study has found some important differences between women in different age groups.

Adolescent women in the sample were found to be at significantly increased risk of delivering babies with extremely low birth weights after adjustment for confounding factors. Extremely low birthweight is often associated with premature delivery which was not detected in this study. This is however likely to be due to the low power of the study to detect differences in rare events such as this outcome. Identifying the higher risk of delivering babies with an extremely low birthweight is of particular importance due to its association with neonatal mortality and morbidity. Babies with ELBW are more likely to die in the first few months of life [16] and are more likely to have long lasting physical and cognitive developmental issues [17] compared to babies born at higher weights.

The sub-group analysis of the youngest women in the sample identified an increased risk of pre-eclampsia in this group. Pre-eclamsia is a hypertensive disorder [18] and is a major cause of maternal morbidity and mortality worldwide.[19] While mortality in developed countries is low, pre-eclampsia has also been associated with severe maternal morbidity such as strokes and adverse neonatal outcomes such as prematurity and intrauterine growth restriction.[19] Pre-eclampsia is also indicated as a marker for increased risk of cardiovascular and metabolic diseases later in life.[20] This is an important finding which could have implications for the health of young mothers and their babies. Further research to examine the causal mechanisms leading to the increased vulnerability to these adverse outcomes in this group to inform targeted prevention methods would be advantageous.

Women aged 35 and over were found to be at significantly higher risk of caesarean and instrumental delivery, the sub-group analysis also showed increased risk of caesarean in women aged 40 and over. Caesarean delivery is associated with higher rates of post-natal complications and increased recovery time for the mother.[21] Instrumental deliveries, while necessary to prevent serious neonatal complications, are associated with a higher prevalence of birth injuries and maternal rehospitalisation.[22] These results are consistent with a large body of existing work where these outcomes have been found to be associated with maternal age.[23-25] It is not known whether these differences are due to biological differences between younger and older women or whether the reasons are more likely to be social or cultural. Further investigation regarding the reasons for difference in mode of birth in women of different ages would be advantageous.

The results of this study also added to the body of evidence associating gestational diabetes with advancing maternal age. Age was shown to be an independent factor in this cohort after controlling for the effect of BMI which is a well-established predictor of gestational diabetes risk. Gestational diabetes is associated with both immediate and longer term complications such as macrosomia, shoulder dystocia and birth injuries in the short term and increased risk of obesity and impairment of glucose tolerance (leading to type 2 diabetes) for both mother and child [26].

Sub-group analysis of the oldest women in the cohort (40 years and over) showed some significant concerns for neonatal outcomes, as well as the adverse maternal outcomes shared with women aged 35 and over. The findings for this group showed that the risk of APGAR score under 7 at 5 minutes, low birthweight, prematurity and stillbirth were all significantly high compared to the reference group. Increased risk of

adverse neonatal outcomes in older women has been previously evidenced;[24,27-28] these results therefore are consistent with the existing literature in this field.

Comparison of the results of this study to key indicators published by Public Health England's Child and Maternal Health Intelligence Network [29] suggests that despite the uniqueness of this cohort the results are generalisable to other areas of the UK. Reported national rates for smoking in pregnancy, low birth weight and stillbirth are similar both among the adolescent population and the population as a whole to those reported in this study.

The results of this study contribute to the wider understanding of neonatal and maternal morbidity and mortality both in a UK context and internationally. This study identifies important differences in the risk of adverse outcomes by maternal age, which align with the United Nations sustainable development goals [30] and the targets outlined in the Every Woman, Every Child Global Strategy.[31] Pre-term births and low birth weights are a major cause of neonatal death and cause more than 1 million deaths globally per year and hypertensive disorders are the second leading cause of maternal mortality.[31] In addition to this the second leading cause of death for young women aged 15-19 years is complications during pregnancy and childbirth.[32] Identifying characteristics which put individuals at higher risk of these complications will help in targeting interventions to populations which are appropriate to their setting.

A significant strength of this study is that it utilises a large cohort study meaning that the majority of statistical analyses do not suffer from problems due to small numbers. This said there were still only a very small number of very young women (under 16) in the cohort meaning that effect of age on outcomes in this group may have failed to

be detected. Stillbirth, premature deliveries and very and extremely low birthweights were also still relatively rare events, meaning these analyses may have been more robust with larger numbers.

There was also a significant amount of missing data for some variables, particularly alcohol use during pregnancy, questions about which having been answered by less than a third of the sample. This missing data made it impractical to adjust the regression models by alcohol use which has previously been associated with adverse neonatal outcomes. [9]

CONCLUSIONS

This study identifies some important variations in obstetric and perinatal outcomes by maternal age. Extremely low birth weight was a concern for adolescent mothers with risk of pre-eclampsia also being higher in the youngest adolescents (≤16). Findings relating to outcomes for older women were consistent with the existing literature showing higher risk of gestational diabetes and caesarean delivery. Women in the oldest age group were also at higher risk of adverse neonatal outcomes. Further work to establish the causal mechanisms behind the links between maternal age and mode of birth would be advantageous, particularly for adolescent mothers where there are significant gaps in the existing literature.

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COMPETING INTERESTS

The authors declare that they have no competing interests

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AUTHOR'S CONTRIBUTIONS

Katie Marvin-Dowle: Completion of data analysis and responsible for writing the manuscript.

Karen Kilner: Providing specialist input on statistical methods

Victoria Burley: Providing specialist input on methods and structure, providing comments and making amendments to the manuscript.

Hora Soltani: Providing specialist input on methods and structure, providing comments and making amendments to the manuscript.

ACCESS TO DATA

Requests for access to data should be addressed to the corresponding author or to the Born in Bradford programme manager rosie.mceachan@bthft.nhs.uk

REFERENCES

[1] Cook SMC, Cameron ST. Social issues of teenage pregnancy. *Obstetrics, Gynaecology & Reproductive Medicine*. 2015; 25(9):243-8
[2] Gilbert WM. Jandial D. Field NT. Birth outcomes in teenage pregnancies. *J Matern Fetal Neonatal Med*. 2004;16(5):265-270.
[3] Tyrberg RB, Blomberg M, Kjolhede P. Deliveries among teenage women - with emphasis on incidence and mode of delivery: A swedish national survey from 1973 to 2010. *BMC Pregnancy Childbirth*. 2013; 9;13(1):1
[4] Mohsin M, Bauman A, Jalaludin B. The influence of antenatal and maternal factors on stillbirths and neonatal deaths in New South Wales, Australia. *J Biosoc Sci.* 2006; 38(05):643-57
[5] Blomberg M. Tyrberg RB. Kjolhede P. Impact of maternal age on obstetric and neonatal outcome with emphasis on primiparous adolescents and older women: A swedish medical birth register study. *BMJ Open*. 2014;4(11):e005840.
[6] Kenny, L. C., Lavender, T., McNamee, R., et.al. Advanced maternal age and adverse pregnancy outcome: evidence from a large contemporary cohort, 2013; 8(2):e56583
[7] Gibbs CM, Wendt A, Peters S, et.al The impact of early age at first childbirth on maternal and infant health. *Paediatr Perinat Epidemiol*. 2012;26:259-284.
[8] Pollack, H., Lantz, P. M., Frohna, J. G. Maternal smoking and adverse birth outcomes among singletons and twins. *American Journal of Public Health*, 2000;90(3), 395.
[9] Jaddoe, V. W., Bakker, R., Hofman, A., Mackenbach, J. P., Moll, H. A., Steegers, E. A., & Witteman, J. C. Moderate alcohol consumption during pregnancy and the risk of low birth weight and preterm birth. The generation R study. *Ann Epidemiol*, 2007; 17(10), 834-840.
[10] Blumenshine, P., Egerter, S., Barclay, C. J.,et.al A. Socioeconomic disparities in adverse birth outcomes: a systematic review. *Am J Prev Med*, 2010;*39*(3), 263-272.
[11] East, P. L., & Felice, M. E. Adolescent pregnancy and parenting: Findings from a racially diverse sample. Psychology Press.2014
[12] Wright, J., Small, N., Raynor, P., et.al Cohort profile: the Born in Bradford multi-ethnic family cohort study. *Int J Epidemiol*,2013; 42(4), 978-991.
[13] West, J., Lawlor, D. A., Fairley, L., Wright, J.. Differences in socioeconomic position, lifestyle and health-related pregnancy characteristics between Pakistani and White British women in the Born in Bradford prospective cohort study: the influence of the woman's, her partner's and their parents' place of birth. *BMJ open*, 2014;4(6), e004805.
[14] Fairley, L., Petherick, E. S., Howe, L. D., et.al. Describing differences in weight and length growth trajectories between white and Pakistani infants in the UK: analysis of the Born in Bradford birth cohort study using multilevel linear spline models.*Archives of disease in childhood*, 2013; archdischild-2012.

[15] Lawlor DA, West J, Fairley L, et.al.Pregnancy glycaemia and cord-blood levels of insulin and leptin in Pakistani and white British mother–offspring pairs: findings from a prospective pregnancy cohort. *Diabetologia*. 2014;57(12):2492-500.
[16] Saugstad, O. D., Aune, D. Optimal oxygenation of extremely low birth weight infants: a meta-analysis and systematic review of the oxygen saturation target studies. *Neonatology*, 2013;*105*(1), 55-63.
[17] Dos Santos, E. S. L., De Kieviet, J. F., Königs, M., et.al. Predictive value of the Bayley scales of infant development on development of very preterm/very low birth weight children: a meta-analysis. *Early Hum. Dev.*, 2013;*89*(7), 487-496.
[18] Milne F., Redman C., Walker J., et al.The pre-eclampsia community guideline (PRECOG): how to screen for and detect onset of pre-eclampsia in the community *BMJ*, 2005; 330, 576–580
[19] Duley L., The global impact of pre-eclampsia and eclampsia Semin Perinatol, 2009; 33, 130–137
[20] Bellamy L., Casas JP., Hingorani AD., Pre-eclampsia and risk of cardiovascular disease and cancer in later life: systematic review and meta-analysis *BMJ*, 2007; 335, 974
[21] Van Ham, M. A., Van Dongen, P. W., Mulder, J. Maternal consequences of caesarean section. A retrospective study of intra-operative and postoperative maternal complications of caesarean section during a 10-year period. *European Journal of Obstetrics & Gynecology and Reproductive Biology*, 1997;*74*(1), 1-6.
[22] Lydon-Rochelle, M., Holt, V. L., Martin, D. P.,et.al. Association between method of delivery and maternal rehospitalization.*Jama*, 2000;*283*(18), 2411-2416.
[23] Jolly, M., Sebire, N., Harris, J., et.al The risks associated with pregnancy in women aged 35 years or older. *Hum. Reprod.*,2000; 15(11), 2433-2437.
[24] Jacobsson, B., Ladfors, L., Milsom, I. Advanced maternal age and adverse perinatal outcome. *Obstet Gynecol*, 2004;*104*(4), 727-733.
[25] Freinkel, N., Metzger, B. E., Phelps, R. L., Gestational diabetes mellitus: heterogeneity of maternal age, weight, insulin secretion, HLA antigens, and islet cell antibodies and the impact of maternal metabolism on pancreatic B-cell and somatic development in the offspring. *Diabetes*, 1985;*34*(Supplement 2), 1-7.
[26] Crowther, C. A., Hiller, J. E., Moss, J. R., et.al Effect of treatment of gestational diabetes mellitus on pregnancy outcomes. *N Engl J Med,* 2005;352(24), 2477-2486.
[27] Jahromi, B. N., Husseini, Z. Pregnancy outcome at maternal age 40 and older. *Taiwanese Journal of Obstetrics and Gynecology*, 2008;*47*(3), 318-321.
[28] Flenady, V., Koopmans, L., Middleton, P.,et.al Major risk factors for stillbirth in high-income countries: a systematic review and meta-analysis. *The Lancet*, 2011;377(9774), 1331-1340.
[29] Public Health England, Teenage Parent Outcomes Modelling Tool, available from http://www.chimat.org.uk/teenconceptions/chimattools, date accessed 12.12.16

[30] United Nations, Sustainable Development Goals, available from http://www.undp.org/content/undp/en/home/sustainable-development-goals.html, date accessed 12.12.16

[31] Child EW. Global Strategy for Women's, Children's and Adolescents' Health. New York, NY: Every Woman Every Child. 2015.

[32] World Health Organisation, Adolescent Pregnancy Fact Sheet, available from http://www.who.int/mediacentre/factsheets/fs364/en/ , accessed 12.12.16

STROBE Statement—Checklist of items that should be included in reports of ***cohort studies***

	Item No	Recommendation	Page No.
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	2
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3-5
Objectives	3	State specific objectives, including any pre-specified hypotheses	5
Methods			
Study design	4	Present key elements of study design early in the paper	6-7
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	6
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	6
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed	NA
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6-8
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	6-7
Bias	9	Describe any efforts to address potential sources of bias	7-8
Study size	10	Explain how the study size was arrived at	6
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	6-8
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	7-8
		(*b*) Describe any methods used to examine subgroups and interactions	8
		(*c*) Explain how missing data were addressed	8
		(*d*) If applicable, explain how loss to follow-up was addressed	NA
		(*e*) Describe any sensitivity analyses	NA
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	10, 13, 15,17
		(b) Give reasons for non-participation at each stage	NA
		(c) Consider use of a flow diagram	NA
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	10-11
		(b) Indicate number of participants with missing data for each variable of interest	10-11, 13
		(c) Summarise follow-up time (eg, average and total amount)	NA
Outcome data	15*	Report numbers of outcome events or summary measures over time	13,

			15,17
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	15,17
		(*b*) Report category boundaries when continuous variables were categorized	6-8
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	NA
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	16-17
Discussion			
Key results	18	Summarise key results with reference to study objectives	18-19
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	20-21
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	19-20
Generalisability	21	Discuss the generalisability (external validity) of the study results	20
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	22

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.

BMJ Open

Impact of adolescent age on maternal and neonatal outcomes in the Born in Bradford Cohort

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Impact of adolescent age on maternal and neonatal outcomes in the Born in Bradford Cohort

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Word count: 4,933

ABSTRACT

Objectives: Explore associations between maternal and neonatal outcomes and maternal age, with particular reference to adolescent women.

Design: Population based cohort study

Setting: Maternity department of a large hospital in northern England

Participants: Primiparous women delivering a singleton at Bradford Royal Infirmary between March 2007 and December 2010 aged ≤19 years (N=640) or 20-34 years (N=3951)Sub-group analysis was performed using women aged ≤16 years(N=68). Women aged 20-34 years were used as the reference group.

Primary outcome measures: Maternal and neonatal outcomes

Results: The odds of extremely low birthweight (<1000g) were significantly higher in the adolescent group (≤19 years) compared to the reference group (aOR 4.13, CI 1.41 to 12.11). The odds of very (<32 weeks) and extremely (<28 weeks) pre-term delivery were also higher in the adolescent group (aOR 2.12, CI 1.06 to 4.25 and aOR 5.06, CI 1.23 to 20.78 respectively.

Women in the adolescent group had lower odds of gestational diabetes (aOR 0.35, CI 0.20 to 0.62), caesarean delivery (aOR 0.53, CI 0.42 to 0.67 and instrumental delivery (aOR 0.53 (0.41 to 0.67).

Conclusions: This study identifies important differences in maternal and neonatal outcomes between women by age group. These findings could help in identifying at risk groups for additional support and tailored interventions to minimise the risk of adverse outcomes for these vulnerable groups. Further work is needed to identify the causal mechanisms linking age with outcomes in adolescent women where significant gaps in the literature exist.

Key words: Adolescents; Adults; Women; Pregnancy; Outcomes; Born in Bradford

STRENGTHS AND LIMITATIONS OF THIS STUDY

- A particular strength of this work is that it utilises well-established, ethnically diverse, UK based cohort data in a way which is unique to this study.
- A further strength is in the large number of participants available for analysis which enables robust conclusions to be drawn.

- Despite the large number of participants however, this study is limited by small numbers of occurrences of some rare outcomes, particularly in sub-group analyses.
- It should also be considered that the generalisability of this study to contexts which are very different in terms of socioeconomic and demographic characteristics is limited.

INTRODUCTION

Pregnancy during adolescence is often associated with less favourable outcomes for both mother and child. Childbearing in adolescence is associated with social problems such as isolation, poverty, low levels of education and unemployment.[1]

The impact of maternal age on obstetric and neonatal outcomes has been studied in various parts of the world and with variable results. A WHO multi-country study including 29 low and middle income countries [2] found adolescent mothers were at higher risk of several adverse outcomes including low birthweight, pre-term delivery eclampsia and infections compared to mothers aged 20-24. Similarly in higher income countries there is evidence to suggest that health outcomes may be less favourable for younger mothers. A number of studies have suggested that babies born to adolescent mothers are at higher risk of premature birth and low birthweight [3-4] and that stillbirth and neonatal mortality may be more prevalent in this group.[5] Adolescents have however been consistently shown to have lower rates of caesarean and instrumental delivery [6] and therefore are at lower risk of complications associated with assisted births. It is not currently clear from the available literature however to what extent differences in birth outcomes between adolescent and adult mothers are predicted by age alone.

A number of studies have suggested that neonatal outcomes are less favourable among babies born to adolescent mothers. A systematic review [7] aiming to assess the relationship between early first childbirth and increased risk of poor pregnancy outcomes found that there was considerable evidence to suggest that very young maternal age (<15 years or less than 2 years after menarche) had a negative effect on both maternal and foetal growth and infant survival. It is suggested that young women who are still themselves growing may compete with the foetus for nutrients, which may in turn impair foetal growth and result in low birth weight babies or babies who are small for their gestational age. The review also found a moderately increased risk of anaemia, premature birth and neonatal mortality associated with young maternal age. Advanced maternal age (35+) has also previously been shown to be an independent risk factor for adverse maternal and neonatal outcomes. [8] This suggests that women aged 20-34 could reasonably be considered as the population less likely to suffer age related pregnancy complications.

Differences in outcomes have also been associated with a demographic and behavioural characteristics. Lifestyle and socio-demographic factors such as smoking,[9] alcohol use [10] and deprivation [11] have all been shown to contribute to less favourable birth outcomes. It is also established that adolescent mothers in high income countries are at higher risk of exhibiting these characteristics. [12] The Born in Bradford study is a cohort of approximately 13,500 children born at Bradford Royal Infirmary between March 2007 and December 2010. The cohort reflects the diversity of the population in Bradford and as such is a largely bi-ethnic sample with high levels of socio-economic deprivation, which presents a unique opportunity to explore any differences in birth outcomes between adolescent and adult women and

the factors which contribute to these differences. A detailed profile of the cohort has been previously published. [13]

Some work has already been carried out looking at maternal and neonatal outcomes in the Born in Bradford cohort, particularly with reference to maternal ethnicity. A study looking at differences in socioeconomic status, lifestyle and health-related pregnancy characteristics between Pakistani and White British women [14] found that White British women were more likely to smoke and have a higher body mass index (BMI) compared to Pakistani women, however Pakistani women were more likely to have gestational diabetes. A further study found that infants born to Pakistani women were lighter at birth compared to those born to White British mothers.[15]

While these studies have shown some interesting associations between maternal and neonatal outcomes and maternal ethnicity, the impact of maternal age on outcomes is yet to be explored in this cohort. The size and diversity of this cohort allow for detailed analysis to be carried out and factors known to impact on maternal and neonatal outcomes to be controlled for, making this study unique in a UK context. For these reasons the primary aim of this investigation is to explore the relationship between maternal and neonatal outcomes and maternal age in the Born in Bradford cohort.

METHODS

Born in Bradford is a prospective cohort study for which participants were recruited during pregnancy. The cohort was originally established in response to concerns regarding the high rates of morbidity and mortality in the city. All women booked for delivery at Bradford Royal Infirmary are offered an oral glucose tolerance test

(OGTT) at 26-28 weeks gestation. Women were invited to participate in the Born in Bradford study when attending this appointment or when attending other antenatal appointments. Informed consent was obtained and women were asked to complete a baseline questionnaire providing data on maternal characteristics. Blood and urine samples were also collected from the mothers as well as cord blood samples collected at birth. Recruitment took place between March 2007 and December 2010 and over 80% of women eligible in this period agreed to take part.[13] This study utilises baseline questionnaire data and hospital maternity data collected by Born in Bradford to examine maternal and neonatal outcomes. Data for this study was limited to primiparous women aged 15-34 at delivery who had a singleton pregnancy meaning that data relating to 4,591 pregnancies were available for this analysis. A flowchart describing the Born in Bradford cohort and the sub-set used for this study is shown in figure 1. Ethical approval for the study was granted by Bradford Research Ethics Committee (ref no. 07/H1302/112).

Figure 1.Details of the Born in Bradford cohort and sub-set used for the present study

Outcome variables

The neonatal outcome variables studied were low birthweight (below 2500g), very low birthweight (below 1500g), extremely low birthweight (below 1000g), macrosomia (birthweight over 4000g), small for gestational age (birthweight lower than the 10th percentile for the sample), large for gestational age (birthweight higher than the 90th percentile for the sample), pre-term birth (<37 completed weeks gestation), very pre-term birth (<32 completed weeks gestation), extremely pre-term birth (<28 completed weeks gestation), outcome of birth (live birth or stillbirth) and

APGAR score at 1 and 5 minutes (analysed as two groups, <7 and 7-10). The maternal outcome variables included in this analysis were diagnosis of pre-eclampsia (diagnosis in this cohort was made when proteinuria is >0.3mgs and blood pressure is ≥140/90 on more than one occasion.), diagnosis of gestational diabetes (defined as a 2 hour post glucose load plasma glucose level of 7.8 mmol/ or a fasting plasma glucose level of 6.1mmol/l),[14] mode of birth (normal vaginal, instrumental (including both forceps and ventouse deliveries) or caesarean section). Distinction between elective and emergency caesarean sections was not available. The outcome variables were collected in the process of routine maternity care and were made available for this analysis via data linkage to questionnaire data.

Statistical Analysis

Outcomes in women aged ≤19 were compared to outcomes for women in the reference group (20-34). Age 20-34 was selected as the reference group as this group is the least likely to suffer age related complications as discussed in the introduction.

Characteristics of the sample were described; presenting categorical variables as percentages and continuous variables as means and standard deviations. This analysis was carried out both for demographic characteristics and for maternal and neonatal outcome variables. Differences between maternal age groups were explored using Chi-Square for categorical data and student's t test for continuous data.

Simple linear regression was calculated to predict both birthweight and gestation to last completed week at delivery based on maternal age at delivery.

Binary logistic regression analyses were used to explore the relationships between maternal age group and the categorical outcome variables. Low, very low and extremely low birthweights and macrosomic infants were compared to infants born weighing 2500g - 4000g, small and large for gestational age infants were compared to appropriate for gestational age infants and those born pre-term or very or extremely pre-term to those born ≥37 completed weeks gestation. Multivariate logistic regression models were then used to adjust these comparisons for confounding variables. Crude and adjusted odds ratios (OR and aOR) are therefore presented with 95% confidence intervals. Index of multiple deprivation (IMD) score and maternal ethnicity (white British, Pakistani or any other ethnicity) were included as covariates in the adjusted analysis. Index of multiple deprivation is the official measure of relative deprivation for small areas in England and combines information from seven domains of deprivation (income, employment, education, health, crime, housing and environment) to give a deprivation score.[16]

In the multivariate logistic regression model for this study there is no clear logical or theoretical basis for assuming any variable to be prior to any other, either in terms of its relevance to the research goal of explaining phenomena, or in terms of a hypothetical causal structure of the data. For this reason a simultaneous model of including independent variables in the multivariate logistic regression model was considered to be most appropriate.

Further sub-group analysis was also undertaken to examine the maternal and neonatal outcomes for young women aged ≤16 compared to the reference group and reported in the same way as the main analysis. Statistical analysis was undertaken using SPSS 24.

RESULTS

Characteristics of the sample

Data were available for 4,591 pregnancies for this analysis; characteristics of the participants included in the study are shown in table 1. The majority of participants in the cohort were aged 20-34 (86.1%) with 13.9% aged 19 or under. The sample overall was made up of 37.7% Pakistani women, 44.4% white British woman and 17.6% women of other ethnicities. Among women aged 19 and under only 16.7% were of Pakistani ethnicity and 70% were white British. Women in the adolescent group were also more likely to have been born in the UK or Ireland (88.1%) compared to the reference group (65.5%). There were other significant variations in the characteristics of the sample by maternal age. Women in the adolescent age group were more likely to not be married or living with a partner, to be expecting their first child and to have completed lower levels of education compared to older women. Women in the adolescent age groups were also more likely to have smoked or used recreational drugs during pregnancy, they were also more likely to have drunk alcohol in the first trimester. Women in the reference group were more likely to be overweight or obese while adolescent women were found to have higher prevalence of underweight. Older women were also more likely to have taken nutritional supplements in the four weeks before questionnaire completion compared to younger women. Analysis of continuous variables showed that IMD score decreased as maternal age increased suggesting adolescent women lived in areas of higher deprivation. Adolescent women also booked with a midwife for antenatal care later than older women; there was a mean difference of 1 week between the two groups.

Table 1 Characteristics of the sample by maternal age

	≤19		20-34		Total		Missing		
	N	%	N	%	N	%	N	%	p=
Whole Cohort	**640**	**13.9**	**3951**	**86.1**	**4591**	**100**			
Ethnicity							**14**	**0.3**	
Pakistani	107	16.7	1623	41.1	1730	37.7			<0.001
White British	448	70.0	1590	40.2	2038	44.4			
Any other ethnicity	85	13.3	724	18.3	809	17.6			
Mother's country of birth							**1**	**0.0**	
UK and Ireland	564	88.1	2588	65.5	3152	68.7			<0.001
South East Asia	41	6.4	984	24.9	1025	22.3			
Eastern Europe	15	2.3	135	3.4	150	3.3			
Other/unknown	20	3.1	243	6.2	263	5.7			
Marital Status							**9**	**0.2**	
Married	87	13.6	2445	61.9	2532	55.2			<0.001
Not married - living with partner	147	23.0	841	21.3	988	21.5			
Single	406	63.4	656	16.6	1062	23.1			
Parents related other than by marriage							**3**	**0.1**	
Yes	76	11.9	988	25.0	1064	23.2			<0.001
No	564	88.1	2960	74.9	3524	76.8			
Highest level of education							**14**	**0.3**	
Less than 5 GCSEs grade A-C or equivalent	231	36.1	553	14.0	784	17.1			<0.001
5 GCSEs grade A-C or equivalent	298	46.6	1121	28.4	1419	30.9			
A-levels or higher	60	9.4	1971	49.9	2031	44.2			
Other/unknown	50	7.8	293	7.4	343	7.5			

Smoked during pregnancy							**7**	**0.2**	
Yes	302	47.2	608	15.4	910	19.8			<0.001
No	338	52.8	3336	84.4	3674	80.0			
Drunk alcohol in the first three months of pregnancy							**2862**	**62.3**	
Yes	185	28.9	698	17.7	883	19.2			0.068
No	140	21.9	702	17.8	842	18.3			
Don't Know	1	0.2	3	0.1	4	0.1			
Drunk alcohol since the fourth month of pregnancy							**2872**	**62.6**	
Yes	89	13.9	478	12.1	567	12.4			0.06
No	233	36.4	916	23.2	1149	25.0			
Don't Know	1	0.2	2	0.1	3	0.1			
Used recreational drugs during pregnancy							**771**	**16.8**	
Yes	29	4.5	47	1.2	76	1.7			<0.001
No	509	79.5	3235	81.9	3744	81.6			
Used any vitamins or iron supplements in the last 4 weeks							**16**	**0.3**	
Yes	152	23.8	1610	40.7	1762	38.4			<0.001
No	487	76.1	2326	58.9	2813	61.3			
BMI Category							**413**	**9**	
Underweight (Below 18.5)	59	9.2	199	5.0	258	5.6			<0.001
Healthy weight (18.5 - 24.9)	368	57.5	1853	46.9	2221	48.4			
Overweight (25 - 29.9)	113	17.7	955	24.2	1068	23.3			
Obese (30 or higher)	46	7.2	585	14.8	631	13.7			
	N	**Mean (SD)**	**N**	**Mean (SD)**	**N**	**Mean (SD)**	**N**	**%**	**p=**
BMI at booking appointment	594	23.3 (4.6)	3641	25.1 (5.4)	4235	24.8 (5.3)	356	7.8	<0.001
IMD Score	640	44.7 (18.0)	3948	41.6 (17.9)	4588	41.8 (17.9)	3	0.1	<0.001
Number of weeks gestation at booking appointment	640	12.1 (5.0)	3951	11.4 (4.3)	4246	12.4 (3.1)	345	7.5	<0.001

Descriptive analysis relating to maternal and neonatal outcomes is shown in table 2. This analysis suggests that there are several outcome variables which show significant variation by maternal age group. Among the neonatal outcomes the results show babies born to adolescent women were significantly more likely to have extremely low birthweights or to be born very or extremely pre-term. Among the maternal outcomes lower rates of gestational diabetes, caesarean delivery and instrumental birth were associated with adolescent age.

Table 2 Descriptive analysis of maternal and neonatal outcomes by maternal age

	≤19		20-34		Total		Missing		
	N	%	N	%	N	%	N	%	p=
Whole Cohort	**640**	**13.9**	**3951**	**86.1**	**4591**	**100**			
Neonatal Outcomes									
Low birthweight (<2500g)	56	9.3	349	9.4	405	9.3	0	0.0	0.933
Very low birthweight (<1500g)	9	1.6	36	1.1	45	1.1	0	0.0	0.248
Extremely low birthweight (<1000g)	6	1.1	10	0.3	16	0.4	0	0.0	0.007
Macrosomia (Birthweight >4000g)	35	6.0	223	6.2	258	6.2	0	0.0	0.852
Small for gestational age	81	14.0	576	16.3	657	16.0	0	0.0	0.153
Large for gestational age	61	10.9	426	12.6	487	12.4	0	0.0	0.256
Pre-term delivery (<37 weeks)	44	6.9	236	6.0	280	6.1	0	0.0	0.376
Very pre-term delivery (<32 weeks)	12	2.0	35	0.9	47	1.1	0	0.0	0.021
Extremely pre-term delivery (<28 weeks)	4	0.7	5	0.1	9	0.2	0	0.0	0.008
Stillborn	5	0.8	26	0.7	31	0.7	0	0.0	0.724
APGAR score <7 at 1 minute	75	11.7	456	11.5	531	11.6	0	0.0	0.896
APGAR score <7 at 5 minutes	24	3.8	136	3.4	160	3.5	0	0.0	0.694
	N	**Mean (SD)**	**N**	**Mean (SD)**	**N**	**Mean (SD)**	**N**	**%**	**p=**
Birthweight (g)	640	3167.6 (580.6)	3950	3183.1 (556.3)	4590	3180.9 (559.7)	1	0.0	0.919
Gestation to last completed week	640	39.2 (2.2)	3951	39.2 (1.9)	4591	39.2 (1.9)	0	0.0	0.516
Maternal Outcomes									
Pre-eclampsia	19	3.0	146	3.7	165	3.6	0	0.0	0.36
Gestational Diabetes	13	2.0	264	6.7	277	6.0	0	0.0	<0.001
Caesarean Delivery	93	14.5	990	25.1	1083	23.6	0	0.0	<0.001
Instrumental birth[¥]	78	14.3	706	23.9	784	22.4	5	0.1	<0.001

¥ Vaginal deliveries only, included both forceps and ventouse deliveries

Linear regression models

A simple linear regression was carried out to assess the relationship between birthweight and maternal age. A statistically significant relationship was found (p=0.044). The slope coefficient for maternal age was 3.749 meaning that for each one year increase in maternal age birthweight increases by 3.749g. The R^2 value was 0.001 meaning that only 0.1% of the variation in birthweight can be explained by the model containing only maternal age.

Similarly a simple linear regression to assess the relationship between gestation at delivery to last completed week and maternal age found a significant relationship (p=0.011). The slope coefficient for maternal age was -0.016 meaning that for each one year increase in maternal age gestation at delivery decreases by 0.016 weeks. The R^2 value for this regression was also 0.001 meaning that only 0.1% of the variation in gestation at delivery can be explained by the model containing only maternal age.

Logistic Regression Analysis

The crude and adjusted odds ratios for maternal and neonatal outcomes by maternal age group are shown in table 3.

Women in the adolescent age group were found to have a significantly higher odds of delivering extremely low birthweight babies (<1000g) compared to the reference group (aOR 4.13, CI 1.41 to 12.11) and delivering extremely pre-term (<28 weeks) (aOR 5.06, CI 1.23 to 20.78). Adolescent pregnant women experienced lower odds of being diagnosed with gestational diabetes than the reference group (aOR 0.35, CI 0.20 to 0.62). The odds of women in this age group delivering by caesarean section

were decreased (aOR 0.53, CI 0.42 to 0.67), as were the odds of having an instrumental delivery (aOR 0.53, CI 0.41 to 0.69) compared to the reference group.

Table 3 Neonatal and maternal outcomes for adolescent women

	N	Crude OR (95% CI)	aOR (95% CI)*
Neonatal Outcomes			
Low birthweight (<2500g)	4332	0.99 (0.73 to 1.33)	1.10 (0.81 to 1.50)
Very low birthweight (<1500g)	3972	1.54 (0.74 to 3.21)	1.59 (0.74 to 3.42)
Extremely low birthweight (<1000g)	3943	3.69 (1.34 to 10.20)	4.13 (1.41 to 12.11)
Macrosomia (Birthweight >4000g)	4185	0.97 (0.67 to 1.40)	0.78 (0.54 to 1.14)
Small for gestational age	4104	0.83 (0.65 to 1.07)	1.05 (0.81 to 1.37)
Large for gestational age	3934	0.85 (0.64 to 1.13)	0.74 (0.55 to 0.99)
Pre-term delivery (<37 weeks)	4591	1.16 (0.83 to 1.62)	1.10 (0.78 to 1.56)
Very pre-term delivery (<32 weeks)	4358	2.14 (1.10 to 4.14)	2.12 (1.06 to 4.25)
Extremely pre-term delivery (<28 weeks)	4320	4.99 (1.34 to 18.62)	5.06 (1.23 to 20.78)
Stillborn	4591	1.19 (0.46 to 3.11)	1.39 (0.51 to 3.80)
APGAR score <7 at 1 minute	4591	1.02 (0.79 to 1.32)	0.95 (0.73 to 1.25)
APGAR score <7 at 5 minutes	4591	1.09 (0.70 to 1.70)	1.11 (0.70 to 1.76)
Maternal Outcomes			
Pre-eclampsia	4591	0.80 (0.49 to 1.30)	0.84 (0.51 to 1.39)
Gestational Diabetes	4591	0.29 (0.17 to 0.51)	0.35 (0.20 to 0.62)
Caesarean Delivery	4591	0.51 (0.40 to 0.64)	0.53 (0.42 to 0.67)
Instrumental birth¥	3503	0.53 (0.41 to 0.69)	0.53 (0.41 to 0.69)

Reference group: Maternal age 20-34 years, *Adjusted for IMD score and ethnicity

¥ Vaginal deliveries only, included both forceps and ventouse deliveries

Sub-group analysis

For some outcomes the number of events occurring in the sub group aged ≤16, was either very small or no events took place. This resulted in either the regression model failing to produce a valid result or the aOR being subject to extremely wide confidence intervals. The results presented do however provide a useful indication of the outcomes which may be important for further investigation. Results of the sub-group analysis are shown in table 4. The only variable to return a significant result in this analysis was for incidence of caesarean section where the odds were lower for women in the ≤16 sub-group (aOR 0.31, CI 0.13 to 0.72).

Table 4 Sub-group analysis of neonatal and maternal outcomes

	N	Crude OR (95% CI)	aOR (95% CI)*
Neonatal Outcomes			
Low birthweight (<2500g)	3792	0.81 (0.32 to 2.02)	0.83 (0.32 to 2.13)
Very low birthweight (<1500g)	3476	3.13 (0.74 to 13.29)	3.00 (0.66 to 13.59)
Extremely low birthweight (<1000g)	3449	5.63 (0.71 to 44.68)	5.90 (0.67 to 51.85)
Macrosomia (Birthweight >4000g)	3664	0.76 (0.24 to 2.43)	0.62 (0.19 to 2.02)
Small for gestational age	3585	0.57 (0.24 to 1.33)	0.74 (0.31 to 1.77)
Large for gestational age	3437	1.03 (0.49 to 2.17)	0.91 (0.42 to 1.95)
Pre-term delivery (<37 weeks)	4019	1.25 (0.50 to 3.14)	1.08 (0.42 to 2.76)
Very pre-term delivery (<32 weeks)	3814	1.69 (0.23 to 12.49)	1.66 (0.21 to 12.88)
Extremely pre-term delivery (<28 weeks)	3784	11.79 (1.36 to 102.41)	6.24 (0.61 to 64.20)
Stillborn	4019	**	**
APGAR score <7 at 1 minute	4019	1.17 (0.58 to 2.37)	1.02 (0.50 to 2.11)
APGAR score <7 at 5 minutes	4019	0.85 (0.21 to 3.51)	0.85 (0.20 to 3.60)
Maternal Outcomes			
Pre-eclampsia	4019	1.63 (0.59 to 4.53)	1.71 (0.59 to 4.91)
Gestational Diabetes	4019	**	**
Caesarean Delivery	4019	0.29 (0.13 to 0.67)	0.31 (0.13 to 0.72)
Instrumental birth¥	3025	0.83 (0.46 to 1.50)	0.87 (0.47 to 1.60)

Reference group: Maternal age 20-34 years, *Adjusted for IMD score and ethnicity **No valid result available due to small numbers

¥ Vaginal deliveries only, included both forceps and ventouse deliveries

DISCUSSION

Analysis of maternal and neonatal outcomes in the Born in Bradford cohort in this study has found some important differences between women in different age groups.

Adolescent women in the sample were found to be at significantly increased risk of delivering babies extremely pre-term and with extremely low birth weights after adjustment for confounding factors. Identifying the risk of delivering babies with an extremely low birthweight is of particular importance due to its association with neonatal mortality and morbidity. Babies with ELBW are more likely to die in the first few months of life [17] and are more likely to have long lasting physical and cognitive developmental issues [18] compared to babies born at higher weights. Extreme low birthweight and extreme pre-term delivery are intrinsically linked and thus morbidity and mortality in extremely pre-term infants is similar to those with extremely low birth weights.[19]

In the UK survival rates for babies born extremely pre-term increase rapidly with each additional week the foetus remains in the womb from close to zero at 22 weeks gestation to 92% at 28 completed weeks,[20] meaning that neonatal death is a significant concern for babies born in this time period. Mortality data were not available for this study for infants who were born alive; this would be an important area for further study to assess how mortality rates in pre-term infants born to adolescent mothers compare to those born to older women.

The linear regression analysis of both birthweight and gestation at delivery showed statistically significant results. This said, the R^2 value for both of these analyses showed that maternal age accounted for only 0.1% of the variation in the analysis

meaning that the clinical importance of this finding is limited. It is likely that there are a number of variables which were either not measured in this study or that are currently unknown in the research literature which contribute to these outcomes.

Adolescent women were also found to be at significantly lower risk of caesarean and instrumental delivery in this analysis. Caesarean delivery is associated with higher rates of post-natal complications and increased recovery time for the mother.[21] Instrumental deliveries, while necessary to prevent serious neonatal complications, are associated with a higher prevalence of birth injuries and maternal rehospitalisation.[22] These results are consistent with a large body of existing work where these outcomes have been found to be associated with maternal age.[23-25] It is not known whether these differences are due to biological differences between younger and older women or whether the reasons are more likely to be social or cultural. Further investigation regarding the reasons for difference in mode of birth in women of different ages would be advantageous. The results of this study are consistent with a number of previous similar studies. Results from a study looking at differences in outcomes between adolescent mothers and an older reference group from the North Western Perinatal Survey [26] found an increased risk of low birthweight and pre-term delivery amongst adolescent mothers. This study also measured the effect of parity on these outcomes and reported and increased effect in the second pregnancies of adolescents. Analysis in the present study was limited to primiparous mothers only in order to control for the impact of parity in comparison with the control group. There were insufficient numbers of multiparous women in the adolescent group to allow for analysis of these as a separate group in this study; however the results of this previous study suggest that by excluding second and

subsequent pregnancies the extent of low birthweight and pre-term delivery may have been underestimated.

A further study [27] comparing adolescent pregnancy outcomes to those of older women found a decreased risk of caesarean section and instrumental delivery in the adolescent group which is consistent with the findings of this study. This study did however fail to find any association with low birth weight or pre-term delivery after adjusting for confounding variables. This analysis did not however look at extreme low birth weight or extreme pre-term delivery which is where the present study has detected differences between groups.

Comparison of the results of this study to key indicators published by Public Health England's Child and Maternal Health Intelligence Network [28] suggests that despite the uniqueness of this cohort the results are generalisable to other areas of the UK. Reported national rates for smoking in pregnancy, low birth weight and stillbirth are similar both among the adolescent population and the population as a whole to those reported in this study.

The results of this study contribute to the wider understanding of neonatal and maternal morbidity and mortality both in a UK context and internationally. This study identifies important differences in the risk of adverse outcomes by maternal age, which align with the United Nations sustainable development goals [29] and the targets outlined in the Every Woman, Every Child Global Strategy.[30] Pre-term births and low birth weights are a major cause of neonatal death and cause more than 1 million deaths globally per year.[31] In addition to this the second leading cause of death for young women aged 15-19 years is complications during pregnancy and childbirth.[31] Identifying characteristics which put individuals at

higher risk of these complications will help in targeting interventions to populations which are appropriate to their setting.

A significant strength of this study is that it utilises a large cohort study meaning that the majority of statistical analyses do not suffer from problems due to small numbers. This said there were still only a very small number of very young women (under 16) in the cohort meaning that effect of age on outcomes in this group may have failed to be detected. Stillbirth, premature deliveries and very and extremely low birthweights were also still relatively rare events, resulting in very wide confidence intervals; these analyses would have been more robust with larger numbers of overall events.

CONCLUSIONS

This study identifies some important variations in obstetric and perinatal outcomes by maternal age. Extremely low birth weight and extremely pre-term delivery were concerns for adolescent mothers. Findings relating to maternal outcomes were also consistent with the existing literature showing lower risk of gestational diabetes, caesarean delivery and instrumental birth. Further work to establish the causal mechanisms behind the links between maternal age and maternal and neonatal outcomes would be advantageous, particularly for adolescent mothers where there are significant gaps in the existing literature.

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COMPETING INTERESTS

The authors declare that they have no competing interests

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AUTHOR'S CONTRIBUTIONS

Katie Marvin-Dowle: Completion of data analysis and responsible for writing the manuscript.

Karen Kilner: Providing specialist input on statistical methods

Victoria Burley: Providing specialist input on methods and structure, providing comments and making amendments to the manuscript.

Hora Soltani: Providing specialist input on methods and structure, providing comments and making amendments to the manuscript.

ACCESS TO DATA

Requests for access to data should be addressed to the corresponding author or to the Born in Bradford programme manager rosie.mceachan@bthft.nhs.uk

REFERENCES

[1] Cook SMC, Cameron ST. Social issues of teenage pregnancy. *Obstetrics, Gynaecology & Reproductive Medicine*. 2015; 25(9):243-8
[2] Ganchimeg T, Ota E, Morisaki N, et.al Pregnancy and childbirth outcomes among adolescent mothers: a World Health Organization multicountry study. *BJOG: An International Journal of Obstetrics & Gynaecology*. 2014 Mar 1;121(s1):40-8.
[3] Gilbert WM. Jandial D. Field NT. Birth outcomes in teenage pregnancies. *J Matern Fetal Neonatal Med*. 2004;16(5):265-270.
[4] Tyrberg RB, Blomberg M, Kjolhede P. Deliveries among teenage women - with emphasis on incidence and mode of delivery: A swedish national survey from 1973 to 2010. *BMC Pregnancy Childbirth*. 2013; 9;13(1):1
[5] Mohsin M, Bauman A, Jalaludin B. The influence of antenatal and maternal factors on stillbirths and neonatal deaths in New South Wales, Australia. *J Biosoc Sci.* 2006; 38(05):643-57
[6] Blomberg M. Tyrberg RB. Kjolhede P. Impact of maternal age on obstetric and neonatal outcome with emphasis on primiparous adolescents and older women: A swedish medical birth register study. *BMJ Open*. 2014;4(11):e005840.
[7] Gibbs CM, Wendt A, Peters S, et.al The impact of early age at first childbirth on maternal and infant health. *Paediatr Perinat Epidemiol*. 2012;26:259-284.
[8] Kenny, L. C., Lavender, T., McNamee, R., et.al. Advanced maternal age and adverse pregnancy outcome: evidence from a large contemporary cohort, 2013; 8(2):e56583
[9] Pollack, H., Lantz, P. M., Frohna, J. G. Maternal smoking and adverse birth outcomes among singletons and twins. *American Journal of Public Health*, 2000;90(3), 395.
[10] Jaddoe, V. W., Bakker, R., Hofman, A., Mackenbach, J. P., Moll, H. A., Steegers, E. A., & Witteman, J. C. Moderate alcohol consumption during pregnancy and the risk of low birth weight and preterm birth. The generation R study. *Ann Epidemiol*, 2007; 17(10), 834-840.
[11] Blumenshine, P., Egerter, S., Barclay, C. J.,et.al A. Socioeconomic disparities in adverse birth outcomes: a systematic review. *Am J Prev Med*, 2010;*39*(3), 263-272.
[12] East, P. L., & Felice, M. E. Adolescent pregnancy and parenting: Findings from a racially diverse sample. Psychology Press.2014
[13] Wright, J., Small, N., Raynor, P., et.al Cohort profile: the Born in Bradford multi-ethnic family cohort study. *Int J Epidemiol*,2013; 42(4), 978-991.
[14] West, J., Lawlor, D. A., Fairley, L., Wright, J.. Differences in socioeconomic position, lifestyle and health-related pregnancy characteristics between Pakistani and White British women in the Born in Bradford prospective cohort study: the influence of the woman's, her partner's and their parents' place of birth. *BMJ open*, 2014;4(6), e004805.
[15] Fairley, L., Petherick, E. S., Howe, L. D., et.al. Describing differences in weight and length growth trajectories between white and Pakistani infants in the UK: analysis of the Born in Bradford birth

cohort study using multilevel linear spline models.*Archives of disease in childhood*, 2013; archdischild-2012.
[16] Office for National Statistics, English indices of deprivation 2015, [online] accessed 17.11.17 available from https://www.gov.uk/government/statistics/english-indices-of-deprivation-2015
[17] Saugstad, O. D., Aune, D. Optimal oxygenation of extremely low birth weight infants: a meta-analysis and systematic review of the oxygen saturation target studies. *Neonatology*, 2013;*105*(1), 55-63.
[18] Dos Santos, E. S. L., De Kieviet, J. F., Königs, M., et.al. Predictive value of the Bayley scales of infant development on development of very preterm/very low birth weight children: a meta-analysis. *Early Hum. Dev.*, 2013;*89*(7), 487-496.
[19] Goldenberg RL, Culhane JF, Iams JD, Romero R. Epidemiology and causes of preterm birth. *The Lancet*. 2008 Jan 11;371(9606):75-84.[20] Tommy's, *Premature Birth Statistics,* [online] accessed 17.11.17 available from https://www.tommys.org/our-organisation/why-we-exist/premature-birth-statistics
[21] Van Ham, M. A., Van Dongen, P. W., Mulder, J. Maternal consequences of caesarean section. A retrospective study of intra-operative and postoperative maternal complications of caesarean section during a 10-year period. *European Journal of Obstetrics & Gynecology and Reproductive Biology*, 1997;*74*(1), 1-6.
[22] Lydon-Rochelle, M., Holt, V. L., Martin, D. P.,et.al. Association between method of delivery and maternal rehospitalization.*Jama*, 2000;*283*(18), 2411-2416.
[23] Jolly, M., Sebire, N., Harris, J., et.al The risks associated with pregnancy in women aged 35 years or older. *Hum. Reprod.*,2000; 15(11), 2433-2437.
[24] Jacobsson, B., Ladfors, L., Milsom, I. Advanced maternal age and adverse perinatal outcome. *Obstet Gynecol*, 2004;*104*(4), 727-733.
[25] Freinkel, N., Metzger, B. E., Phelps, R. L., Gestational diabetes mellitus: heterogeneity of maternal age, weight, insulin secretion, HLA antigens, and islet cell antibodies and the impact of maternal metabolism on pancreatic B-cell and somatic development in the offspring. *Diabetes*, 1985;*34*(Supplement 2), 1-7.
[26] Khashan AS, Baker PN, Kenny LC. Preterm birth and reduced birthweight in first and second teenage pregnancies: a register-based cohort study. *BMC pregnancy and childbirth*. 2010 Jul 9;10(1):36.
[27] De Vienne CM, Creveuil C, Dreyfus M. Does young maternal age increase the risk of adverse obstetric, fetal and neonatal outcomes: a cohort study. *European Journal of Obstetrics & Gynecology and Reproductive Biology*. 2009 Dec 31;147(2):151-6.
[28] Public Health England, Teenage Parent Outcomes Modelling Tool, available from http://www.chimat.org.uk/teenconceptions/chimattools, date accessed 12.12.16

[29] United Nations, Sustainable Development Goals, available from http://www.undp.org/content/undp/en/home/sustainable-development-goals.html, date accessed 12.12.16

[30] Child EW. Global Strategy for Women's, Children's and Adolescents' Health. New York, NY: Every Woman Every Child. 2015.

[31] World Health Organisation, Adolescent Pregnancy Fact Sheet, available from http://www.who.int/mediacentre/factsheets/fs364/en/ , accessed 12.12.16

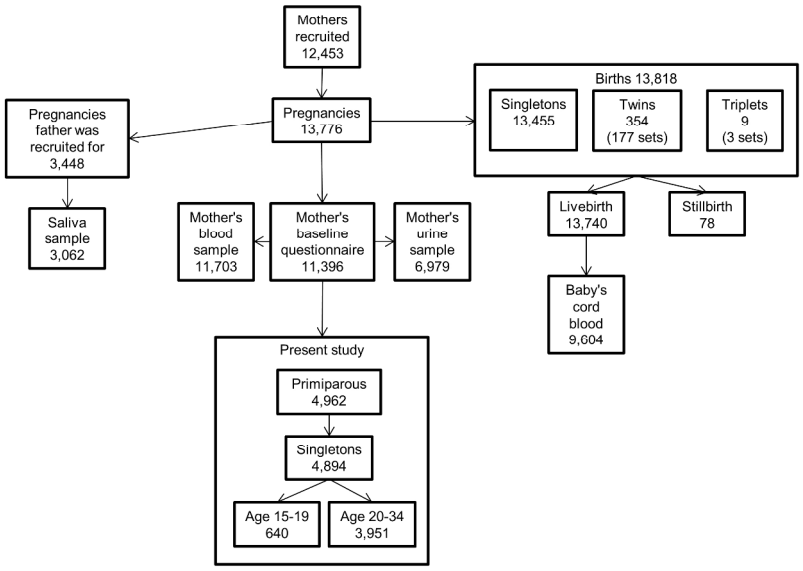

Figure 1.Details of the Born in Bradford cohort and sub-set used for the present study

254x190mm (300 x 300 DPI)

STROBE Statement—Checklist of items that should be included in reports of ***cohort studies***

	Item No	Recommendation	Page No.
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	2
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3-5
Objectives	3	State specific objectives, including any pre-specified hypotheses	5
Methods			
Study design	4	Present key elements of study design early in the paper	6-7
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	6
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	6
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed	NA
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6-8
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	6-7
Bias	9	Describe any efforts to address potential sources of bias	7-8
Study size	10	Explain how the study size was arrived at	6
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	6-8
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	7-8
		(*b*) Describe any methods used to examine subgroups and interactions	8
		(*c*) Explain how missing data were addressed	8
		(*d*) If applicable, explain how loss to follow-up was addressed	NA
		(*e*) Describe any sensitivity analyses	NA
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	10, 13, 16,18
		(b) Give reasons for non-participation at each stage	NA
		(c) Consider use of a flow diagram	NA
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	10-11
		(b) Indicate number of participants with missing data for each variable of interest	10-11, 13
		(c) Summarise follow-up time (eg, average and total amount)	NA
Outcome data	15*	Report numbers of outcome events or summary measures over time	13,

			16,18
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	16,18
		(*b*) Report category boundaries when continuous variables were categorized	6-8
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	NA
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	17-18
Discussion			
Key results	18	Summarise key results with reference to study objectives	19-20
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	21-22
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	20-21
Generalisability	21	Discuss the generalisability (external validity) of the study results	21
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	23

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.

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Impact of adolescent age on maternal and neonatal outcomes in the Born in Bradford Cohort

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Impact of adolescent age on maternal and neonatal outcomes in the Born in Bradford Cohort

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Word count: 5,014

ABSTRACT

Objectives: Explore associations between maternal and neonatal outcomes and maternal age, with particular reference to adolescent women.

Design: Population based cohort study

Setting: Maternity department of a large hospital in northern England

Participants: Primiparous women delivering a singleton at Bradford Royal Infirmary between March 2007 and December 2010 aged ≤19 years (N=640) or 20-34 years (N=3951)Sub-group analysis was performed using women aged ≤16 years(N=68). Women aged 20-34 years were used as the reference group.

Primary outcome measures: Maternal and neonatal outcomes

Results: The odds of extremely low birthweight (<1000g) were significantly higher in the adolescent group (≤19 years) compared to the reference group (aOR 4.13, CI 1.41 to 12.11). The odds of very (<32 weeks) and extremely (<28 weeks) pre-term delivery were also higher in the adolescent group (aOR 2.12, CI 1.06 to 4.25 and aOR 5.06, CI 1.23 to 20.78 respectively.

Women in the adolescent group had lower odds of gestational diabetes (aOR 0.35, CI 0.20 to 0.62), caesarean delivery (aOR 0.53, CI 0.42 to 0.67 and instrumental delivery (aOR 0.53 (0.41 to 0.67).

Conclusions: This study identifies important differences in maternal and neonatal outcomes between women by age group. These findings could help in identifying at risk groups for additional support and tailored interventions to minimise the risk of adverse outcomes for these vulnerable groups. Further work is needed to identify the causal mechanisms linking age with outcomes in adolescent women where significant gaps in the literature exist.

Key words: Adolescents; Adults; Women; Pregnancy; Outcomes; Born in Bradford

STRENGTHS AND LIMITATIONS OF THIS STUDY

- A particular strength of this work is that it utilises well-established, ethnically diverse, UK based cohort data in a way which is unique to this study.
- A further strength is in the large number of participants available for analysis which enables robust conclusions to be drawn.

- Despite the large number of participants however, this study is limited by small numbers of occurrences of some rare outcomes, particularly in sub-group analyses.
- It should also be considered that the generalisability of this study to contexts which are very different in terms of socioeconomic and demographic characteristics is limited.

INTRODUCTION

Pregnancy during adolescence is often associated with less favourable outcomes for both mother and child. Childbearing in adolescence is associated with social problems such as isolation, poverty, low levels of education and unemployment.[1]

The impact of maternal age on obstetric and neonatal outcomes has been studied in various parts of the world and with variable results. A WHO multi-country study including 29 low and middle income countries [2] found adolescent mothers were at higher risk of several adverse outcomes including low birthweight, pre-term delivery eclampsia and infections compared to mothers aged 20-24.

Similarly in higher income countries there is evidence to suggest that health outcomes may be less favourable for younger mothers.. Babies born to adolescent mothers have been shown to be at higher risk of pre-term birth and low birthweight [3-4] and higher rates of stillbirth and neonatal mortality have also been reported.[5] Adolescents have however been consistently shown to experience lower rates of caesarean and instrumental delivery [6] and therefore are at lower risk of complications associated with assisted births. It is not currently clear from the

available literature however to what extent differences in birth outcomes between adolescent and adult mothers are predicted by age alone.

A systematic review [7] aiming to assess the relationship between early first childbirth and increased risk of poor pregnancy outcomes found that there was considerable evidence to suggest that very young maternal age (<15 years or less than 2 years after menarche) had a negative effect on both maternal and foetal growth and infant survival. It is suggested that young women who are still themselves growing may compete with the foetus for nutrients, which may in turn impair foetal growth and result in low birth weight babies or babies who are small for their gestational age. The review also found a moderately increased risk of anaemia, premature birth and neonatal mortality associated with young maternal age. Advanced maternal age (35+) has also previously been shown to be an independent risk factor for adverse maternal and neonatal outcomes. [8] This suggests that women aged 20-34 could reasonably be considered as the population less likely to suffer age related pregnancy complications.

Differences in outcomes have also been associated with demographic and behavioural characteristics. Lifestyle and socio-demographic factors such as smoking,[9] alcohol use [10] and deprivation [11] have all been shown to contribute to less favourable birth outcomes. It is also established that adolescent mothers in high income countries are at higher risk of exhibiting these characteristics. [12]

The Born in Bradford study is a cohort of approximately 13,500 children born at Bradford Royal Infirmary between March 2007 and December 2010. The cohort reflects the diversity of the population in Bradford and as such is a largely bi-ethnic sample with high levels of socio-economic deprivation, which presents a unique

opportunity to explore any differences in birth outcomes between adolescent and adult women and the factors which contribute to these differences. A detailed profile of the cohort has been previously published. [13]

Some work has already been carried out looking at maternal and neonatal outcomes in the Born in Bradford cohort, particularly with reference to maternal ethnicity, [14-15] however this cohort has not previously been examined with reference to maternal age.

While these studies have shown some interesting associations between maternal and neonatal outcomes and maternal ethnicity, the impact of maternal age on outcomes is yet to be explored in this cohort. The size and diversity of this cohort allow for detailed analysis to be carried out and factors known to impact on maternal and neonatal outcomes to be controlled for, making this study unique in a UK context. For these reasons the primary aim of this investigation is to explore the relationship between maternal and neonatal outcomes and maternal age in the Born in Bradford cohort.

METHODS

Born in Bradford is a prospective cohort study for which participants were recruited during pregnancy. The cohort was originally established in response to concerns regarding the high rates of morbidity and mortality in the city. All women booked for delivery at Bradford Royal Infirmary are offered an oral glucose tolerance test (OGTT) at 26-28 weeks gestation. Women were invited to participate in the Born in Bradford study when attending this appointment or when attending other antenatal appointments. Informed consent was obtained and women were asked to complete a baseline questionnaire providing data on maternal characteristics. Blood and urine

samples were also collected from the mothers as well as cord blood samples collected at birth. Recruitment took place between March 2007 and December 2010 and over 80% of women eligible in this period agreed to take part, which represents approximately 64% of the births occurring in Bradford during this period.[13] This study utilises baseline questionnaire data and hospital maternity data collected by Born in Bradford to examine maternal and neonatal outcomes. The youngest women recruited to the cohort were 15 years old, therefore data for this study was limited to primiparous women aged 15-34 at delivery who had a singleton pregnancy; data relating to 4,591 pregnancies were available for this analysis. A flowchart describing the Born in Bradford cohort and the sub-set used for this study is shown in figure 1. Ethical approval for the study was granted by Bradford Research Ethics Committee (ref no. 07/H1302/112).

Figure 1.Details of the Born in Bradford cohort and sub-set used for the present study

Outcome variables

The binary neonatal outcome variables studied were low birthweight (below 2500g), very low birthweight (below 1500g), extremely low birthweight (below 1000g), macrosomia (birthweight over 4000g), small for gestational age (birthweight lower than the 10th percentile for the sample), [16] large for gestational age (birthweight higher than the 90th percentile for the sample), [16] pre-term birth (<37 completed weeks gestation), very pre-term birth (<32 completed weeks gestation), extremely pre-term birth (<28 completed weeks gestation), outcome of birth (live birth or stillbirth) and APGAR score at 1 and 5 minutes (analysed as two groups, <7 and 7-10). Low, very low and extremely low birthweights and macrosomic infants were

compared to infants born weighing 2500g - 4000g, small and large for gestational age infants were compared to appropriate for gestational age infants and those born pre-term or very or extremely pre-term to those born ≥37 completed weeks gestation. Birthweight and gestational age at delivery were also considered as continuous variables. The maternal outcome variables included in this analysis were diagnosis of pre-eclampsia (diagnosis in this cohort was made when proteinuria is >0.3mgs and blood pressure is ≥140/90 on more than one occasion.), diagnosis of gestational diabetes (defined as a 2 hour post glucose load plasma glucose level of 7.8 mmol/ or a fasting plasma glucose level of 6.1mmol/l),[14] mode of birth (normal vaginal, instrumental (including both forceps and ventouse deliveries) or caesarean section). Distinction between elective and emergency caesarean sections was not available. The outcome variables were collected in the process of routine maternity care and were made available for this analysis via data linkage to questionnaire data.

Statistical Analysis

Outcomes in women aged ≤19 were compared to outcomes for women in the reference group (20-34). Age 20-34 was selected as the reference group as this group is the least likely to suffer age related complications as discussed in the introduction.

Characteristics of the sample were described; presenting categorical variables as percentages and continuous variables as means and standard deviations. This analysis was carried out both for demographic characteristics and for maternal and neonatal outcome variables. Differences between maternal age groups were

explored using Chi-Square for categorical data and student's t test for continuous data.

Simple linear regression was calculated to predict both birthweight and gestation to last completed week at delivery based on maternal age at delivery.

Logistic regression analyses were used to compare the rate of each of the binary outcome variables for adolescents and the reference group and differences between groups estimated using odds ratios.

Multivariate logistic regression models were then used to adjust these comparisons for confounding variables. Crude and adjusted odds ratios (OR and aOR) are therefore presented with 95% confidence intervals. Index of multiple deprivation (IMD) score and maternal ethnicity (white British, Pakistani or any other ethnicity) were included as covariates in the adjusted analysis. Index of multiple deprivation is the official measure of relative deprivation for small areas in England and combines information from seven domains of deprivation (income, employment, education, health, crime, housing and environment) to give a deprivation score.[17]

In the multivariate logistic regression model for this study there is no clear logical or theoretical basis for assuming any variable to be prior to any other, either in terms of its relevance to the research goal of explaining phenomena, or in terms of a hypothetical causal structure of the data. For this reason a simultaneous model of including independent variables in the multivariate logistic regression model was considered to be most appropriate.

Further sub-group analysis was also undertaken to examine the maternal and neonatal outcomes for young women aged ≤16 compared to the reference group

and reported in the same way as the main analysis. Statistical analysis was undertaken using SPSS 24.

RESULTS

Characteristics of the sample

Data were available for 4,591 pregnancies for this analysis; characteristics of the participants included in the study are shown in table 1. The majority of participants in the cohort were aged 20-34 (86.1%) with 13.9% aged 19 or under. The sample overall was made up of 37.7% Pakistani women, 44.4% white British woman and 17.6% women of other ethnicities. Among women aged 19 and under only 16.7% were of Pakistani ethnicity and 70% were white British. Women in the adolescent group were also more likely to have been born in the UK or Ireland (88.1%) compared to the reference group (65.5%). There were other significant variations in the characteristics of the sample by maternal age. Women in the adolescent age group were more likely to not be married or living with a partner, to be expecting their first child and to have completed lower levels of education compared to older women. Women in the adolescent age groups were also more likely to have smoked or used recreational drugs during pregnancy; they were also more likely to have drunk alcohol in the first trimester. Women in the reference group were more likely to be overweight or obese while adolescent women were found to have higher prevalence of underweight. Older women were also more likely to have taken nutritional supplements in the four weeks before questionnaire completion compared to younger women. Analysis of continuous variables showed that IMD score decreased as maternal age increased suggesting adolescent women lived in areas of higher deprivation. Adolescent women also booked with a midwife for antenatal

care later than older women; there was a mean difference of 1 week between the two groups.

Table 1 Characteristics of the sample by maternal age

	≤19		20-34		Total		Missing		
	N	%	N	%	N	%	N	%	p=
Whole Cohort	**640**	**13.9**	**3951**	**86.1**	**4591**	**100**			
Ethnicity							**14**	**0.3**	
Pakistani	107	16.7	1623	41.1	1730	37.7			<0.001
White British	448	70.0	1590	40.2	2038	44.4			
Any other ethnicity	85	13.3	724	18.3	809	17.6			
Mother's country of birth							**1**	**0.0**	
UK and Ireland	564	88.1	2588	65.5	3152	68.7			<0.001
South East Asia	41	6.4	984	24.9	1025	22.3			
Eastern Europe	15	2.3	135	3.4	150	3.3			
Other/unknown	20	3.1	243	6.2	263	5.7			
Marital Status							**9**	**0.2**	
Married	87	13.6	2445	61.9	2532	55.2			<0.001
Not married - living with partner	147	23.0	841	21.3	988	21.5			
Single	406	63.4	656	16.6	1062	23.1			
Parents related other than by marriage							**3**	**0.1**	
Yes	76	11.9	988	25.0	1064	23.2			<0.001
No	564	88.1	2960	74.9	3524	76.8			
Highest level of education							**14**	**0.3**	
Less than 5 GCSEs grade A-C or equivalent	231	36.1	553	14.0	784	17.1			<0.001
5 GCSEs grade A-C or equivalent	298	46.6	1121	28.4	1419	30.9			
A-levels or higher	60	9.4	1971	49.9	2031	44.2			
Other/unknown	50	7.8	293	7.4	343	7.5			

Smoked during pregnancy							**7**	**0.2**	
Yes	302	47.2	608	15.4	910	19.8			<0.001
No	338	52.8	3336	84.4	3674	80.0			
Drunk alcohol in the first three months of pregnancy							**2862**	**62.3**	
Yes	185	28.9	698	17.7	883	19.2			0.068
No	140	21.9	702	17.8	842	18.3			
Don't Know	1	0.2	3	0.1	4	0.1			
Drunk alcohol since the fourth month of pregnancy							**2872**	**62.6**	
Yes	89	13.9	478	12.1	567	12.4			0.06
No	233	36.4	916	23.2	1149	25.0			
Don't Know	1	0.2	2	0.1	3	0.1			
Used recreational drugs during pregnancy							**771**	**16.8**	
Yes	29	4.5	47	1.2	76	1.7			<0.001
No	509	79.5	3235	81.9	3744	81.6			
Used any vitamins or iron supplements in the last 4 weeks							**16**	**0.3**	
Yes	152	23.8	1610	40.7	1762	38.4			<0.001
No	487	76.1	2326	58.9	2813	61.3			
BMI Category							**413**	**9**	
Underweight (Below 18.5)	59	9.2	199	5.0	258	5.6			<0.001
Healthy weight (18.5 - 24.9)	368	57.5	1853	46.9	2221	48.4			
Overweight (25 - 29.9)	113	17.7	955	24.2	1068	23.3			
Obese (30 or higher)	46	7.2	585	14.8	631	13.7			
	N	**Mean (SD)**	**N**	**Mean (SD)**	**N**	**Mean (SD)**	**N**	**%**	**p=**
BMI at booking appointment	594	23.3 (4.6)	3641	25.1 (5.4)	4235	24.8 (5.3)	356	7.8	<0.001
IMD Score	640	44.7 (18.0)	3948	41.6 (17.9)	4588	41.8 (17.9)	3	0.1	<0.001
Number of weeks gestation at booking appointment	640	12.1 (5.0)	3951	11.4 (4.3)	4246	12.4 (3.1)	345	7.5	<0.001

Descriptive analysis relating to maternal and neonatal outcomes is shown in table 2. This analysis suggests that there are several outcome variables which show significant variation by maternal age group. Among the neonatal outcomes the results show babies born to adolescent women were significantly more likely to have extremely low birthweights or to be born very or extremely pre-term. Among the maternal outcomes lower rates of gestational diabetes, caesarean delivery and instrumental birth were associated with adolescent age.

Table 2 Descriptive analysis of maternal and neonatal outcomes by maternal age

	≤19		20-34		Total		Missing		
	N	%	N	%	N	%	N	%	p=
Whole Cohort	**640**	**13.9**	**3951**	**86.1**	**4591**	**100**			
Neonatal Outcomes									
Low birthweight (<2500g)	56	9.3	349	9.4	405	9.3	0	0.0	0.933
Very low birthweight (<1500g)	9	1.6	36	1.1	45	1.1	0	0.0	0.248
Extremely low birthweight (<1000g)	6	1.1	10	0.3	16	0.4	0	0.0	0.007
Macrosomia (Birthweight >4000g)	35	6.0	223	6.2	258	6.2	0	0.0	0.852
Small for gestational age	81	14.0	576	16.3	657	16.0	0	0.0	0.153
Large for gestational age	61	10.9	426	12.6	487	12.4	0	0.0	0.256
Pre-term delivery (<37 weeks)	44	6.9	236	6.0	280	6.1	0	0.0	0.376
Very pre-term delivery (<32 weeks)	12	2.0	35	0.9	47	1.1	0	0.0	0.021
Extremely pre-term delivery (<28 weeks)	4	0.7	5	0.1	9	0.2	0	0.0	0.008
Stillborn	5	0.8	26	0.7	31	0.7	0	0.0	0.724
APGAR score <7 at 1 minute	75	11.7	456	11.5	531	11.6	0	0.0	0.896
APGAR score <7 at 5 minutes	24	3.8	136	3.4	160	3.5	0	0.0	0.694
	N	**Mean (SD)**	**N**	**Mean (SD)**	**N**	**Mean (SD)**	**N**	**%**	**p=**
Birthweight (g)	640	3167.6 (580.6)	3950	3183.1 (556.3)	4590	3180.9 (559.7)	1	0.0	0.919
Gestation to last completed week	640	39.2 (2.2)	3951	39.2 (1.9)	4591	39.2 (1.9)	0	0.0	0.516
Maternal Outcomes									
Pre-eclampsia	19	3.0	146	3.7	165	3.6	0	0.0	0.36
Gestational Diabetes	13	2.0	264	6.7	277	6.0	0	0.0	<0.001
Caesarean Delivery	93	14.5	990	25.1	1083	23.6	0	0.0	<0.001
Instrumental birth[¥]	78	14.3	706	23.9	784	22.4	5	0.1	<0.001

¥ Vaginal deliveries only, included both forceps and ventouse deliveries

Linear regression models

A simple linear regression was carried out to assess the relationship between birthweight and maternal age. A statistically significant relationship was found (p=0.044). The slope coefficient for maternal age was 3.749 meaning that for each one year increase in maternal age birthweight increases by 3.749g. The R^2 value was 0.001 meaning that only 0.1% of the variation in birthweight can be explained by the model containing only maternal age.

Similarly a simple linear regression to assess the relationship between gestation at delivery to last completed week and maternal age found a significant relationship (p=0.011). The slope coefficient for maternal age was -0.016 meaning that for each one year increase in maternal age gestation at delivery decreases by 0.016 weeks. The R^2 value for this regression was also 0.001 meaning that only 0.1% of the variation in gestation at delivery can be explained by the model containing only maternal age.

Logistic Regression Analysis

The crude and adjusted odds ratios for maternal and neonatal outcomes by maternal age group are shown in table 3.

Women in the adolescent age group were found to have a significantly higher odds of delivering extremely low birthweight babies (<1000g) compared to the reference group (aOR 4.13, CI 1.41 to 12.11) and delivering extremely pre-term (<28 weeks) (aOR 5.06, CI 1.23 to 20.78). Adolescent pregnant women experienced lower odds of being diagnosed with gestational diabetes than the reference group (aOR 0.35, CI 0.20 to 0.62). The odds of women in this age group delivering by caesarean section

were decreased (aOR 0.53, CI 0.42 to 0.67), as were the odds of having an instrumental delivery (aOR 0.53, CI 0.41 to 0.69) compared to the reference group.

Table 3 Neonatal and maternal outcomes for adolescent women

	N	Crude OR (95% CI)	aOR (95% CI)*
Neonatal Outcomes			
Low birthweight (<2500g)	4332	0.99 (0.73 to 1.33)	1.10 (0.81 to 1.50)
Very low birthweight (<1500g)	3972	1.54 (0.74 to 3.21)	1.59 (0.74 to 3.42)
Extremely low birthweight (<1000g)	3943	3.69 (1.34 to 10.20)	4.13 (1.41 to 12.11)
Macrosomia (Birthweight >4000g)	4185	0.97 (0.67 to 1.40)	0.78 (0.54 to 1.14)
Small for gestational age	4104	0.83 (0.65 to 1.07)	1.05 (0.81 to 1.37)
Large for gestational age	3934	0.85 (0.64 to 1.13)	0.74 (0.55 to 0.99)
Pre-term delivery (<37 weeks)	4591	1.16 (0.83 to 1.62)	1.10 (0.78 to 1.56)
Very pre-term delivery (<32 weeks)	4358	2.14 (1.10 to 4.14)	2.12 (1.06 to 4.25)
Extremely pre-term delivery (<28 weeks)	4320	4.99 (1.34 to 18.62)	5.06 (1.23 to 20.78)
Stillborn	4591	1.19 (0.46 to 3.11)	1.39 (0.51 to 3.80)
APGAR score <7 at 1 minute	4591	1.02 (0.79 to 1.32)	0.95 (0.73 to 1.25)
APGAR score <7 at 5 minutes	4591	1.09 (0.70 to 1.70)	1.11 (0.70 to 1.76)
Maternal Outcomes			
Pre-eclampsia	4591	0.80 (0.49 to 1.30)	0.84 (0.51 to 1.39)
Gestational Diabetes	4591	0.29 (0.17 to 0.51)	0.35 (0.20 to 0.62)
Caesarean Delivery	4591	0.51 (0.40 to 0.64)	0.53 (0.42 to 0.67)
Instrumental birth¥	3503	0.53 (0.41 to 0.69)	0.53 (0.41 to 0.69)

Reference group: Maternal age 20-34 years, *Adjusted for IMD score and ethnicity

¥ Vaginal deliveries only, included both forceps and ventouse deliveries

Sub-group analysis

For some outcomes the number of events occurring in the sub group aged ≤16, was either very small or no events took place. This resulted in either the regression model failing to produce a valid result or the aOR being subject to extremely wide confidence intervals. The results presented do however provide a useful indication of the outcomes which may be important for further investigation. Results of the sub-group analysis are shown in table 4. The only variable to return a significant result in this analysis was for incidence of caesarean section where the odds were lower for women in the ≤16 sub-group (aOR 0.31, CI 0.13 to 0.72).

Table 4 Sub-group analysis of neonatal and maternal outcomes

	N ≤16	N 20-34	Total Valid N	Crude OR (95% CI)	aOR (95% CI)*
	68	**3951**			
Neonatal Outcomes					
Low birthweight (<2500g)	5	349	3792	0.81 (0.32 to 2.02)	0.83 (0.32 to 2.13)
Very low birthweight (<1500g)	2	36	3476	3.13 (0.74 to 13.29)	3.00 (0.66 to 13.59)
Extremely low birthweight (<1000g)	1	10	3449	5.63 (0.71 to 44.68)	5.90 (0.67 to 51.85)
Macrosomia (Birthweight >4000g)	3	223	3664	0.76 (0.24 to 2.43)	0.62 (0.19 to 2.02)
Small for gestational age	6	576	3585	0.57 (0.24 to 1.33)	0.74 (0.31 to 1.77)
Large for gestational age	8	426	3437	1.03 (0.49 to 2.17)	0.91 (0.42 to 1.95)
Pre-term delivery (<37 weeks)	5	236	4019	1.25 (0.50 to 3.14)	1.08 (0.42 to 2.76)
Very pre-term delivery (<32 weeks)	1	35	3814	1.69 (0.23 to 12.49)	1.66 (0.21 to 12.88)
Extremely pre-term delivery (<28 weeks)	1	5	3784	11.79 (1.36 to 102.41)	6.24 (0.61 to 64.20)
Stillborn	0	26	4019	**	**
APGAR score <7 at 1 minute	9	456	4019	1.17 (0.58 to 2.37)	1.02 (0.50 to 2.11)
APGAR score <7 at 5 minutes	2	136	4019	0.85 (0.21 to 3.51)	0.85 (0.20 to 3.60)
Maternal Outcomes					
Pre-eclampsia	4	146	4019	1.63 (0.59 to 4.53)	1.71 (0.59 to 4.91)
Gestational Diabetes	0	264	4019	**	**
Caesarean Delivery	6	990	4019	0.29 (0.13 to 0.67)	0.31 (0.13 to 0.72)
Instrumental birth¥	14	706	3025	0.83 (0.46 to 1.50)	0.87 (0.47 to 1.60)

Reference group: Maternal age 20-34 years, *Adjusted for IMD score and ethnicity **No valid result available due to small numbers

¥ Vaginal deliveries only, included both forceps and ventouse deliveries

DISCUSSION

Analysis of maternal and neonatal outcomes in the Born in Bradford cohort in this study has found some important differences between women in different age groups.

Adolescent women in the sample were found to be at significantly increased risk of delivering babies extremely pre-term and with extremely low birth weights after adjustment for confounding factors. Identifying the risk of delivering babies with an extremely low birthweight is of particular importance due to its association with neonatal mortality and morbidity. Babies with ELBW are more likely to die in the first few months of life [18] and are more likely to have long lasting physical and cognitive developmental issues [19] compared to babies born at higher weights. Extreme low birthweight and extreme pre-term delivery are intrinsically linked and thus morbidity and mortality in extremely pre-term infants is similar to those with extremely low birth weights.[20]

Pre-term deliveries may be clinically indicated due to medical factors such as intrauterine growth restriction or spontaneous. Both spontaneous pre-term delivery [21] and intrauterine growth restriction [22] have been shown to be associated with maternal under nutrition and the links between intrauterine growth restriction and maternal smoking during pregnancy are well established. [21, 23-24] This study has identified a higher prevalence of both maternal underweight and smoking during pregnancy among the adolescent group compared to controls, suggesting that these may be important mechanisms for further investigation in examining the causes of poorer outcomes in adolescent pregnancies.

In the UK survival rates for babies born extremely pre-term increase rapidly with each additional week the foetus remains in the womb from close to zero at 22 weeks gestation to 92% at 28 completed weeks,[25] meaning that neonatal death is a significant concern for babies born in this time period. Mortality data were not available for this study for infants who were born alive; this would be an important area for further study to assess how mortality rates in pre-term infants born to adolescent mothers compare to those born to older women.

The linear regression analysis of both birthweight and gestation at delivery showed statistically significant results. This said, the R^2 value for both of these analyses showed that maternal age accounted for only 0.1% of the variation in the analysis meaning that the clinical importance of this finding is limited. It is likely that there are a number of variables which were either not measured in this study or that are currently unknown in the research literature which contribute to these outcomes.

Adolescent women were also found to be at significantly lower risk of caesarean and instrumental delivery in this analysis. Caesarean delivery is associated with higher rates of post-natal complications and increased recovery time for the mother.[26] Instrumental deliveries, while necessary to prevent serious neonatal complications, are associated with a higher prevalence of birth injuries and maternal rehospitalisation.[27] These results are consistent with a large body of existing work where these outcomes have been found to be associated with maternal age.[28-29] It is not known whether these differences are due to biological differences between younger and older women or whether the reasons are more likely to be social or cultural. Further investigation regarding the reasons for difference in mode of birth in women of different ages would be advantageous. The results of this study are

consistent with a number of previous similar studies. Results from a study looking at differences in outcomes between adolescent mothers and an older reference group from the North Western Perinatal Survey [30] found an increased risk of low birthweight and pre-term delivery amongst adolescent mothers. This study also measured the effect of parity on these outcomes and reported and increased effect in the second pregnancies of adolescents. Analysis in the present study was limited to primiparous mothers only in order to control for the impact of parity in comparison with the control group. There were insufficient numbers of multiparous women in the adolescent group to allow for analysis of these as a separate group in this study; however the results of this previous study suggest that by excluding second and subsequent pregnancies the extent of low birthweight and pre-term delivery may have been underestimated.

A further study [31] comparing adolescent pregnancy outcomes to those of older women found a decreased risk of caesarean section and instrumental delivery in the adolescent group which is consistent with the findings of this study. This study did however fail to find any association with low birth weight or pre-term delivery after adjusting for confounding variables. This analysis did not however look at extreme low birth weight or extreme pre-term delivery which is where the present study has detected differences between groups. Comparison of the results of this study to key indicators published by Public Health England's Child and Maternal Health Intelligence Network [32] suggests that despite the uniqueness of this cohort the results are generalisable to other areas of the UK. Reported national rates for smoking in pregnancy, low birth weight and stillbirth are similar both among the adolescent population and the population as a whole to those reported in this study.

The results of this study contribute to the wider understanding of neonatal and maternal morbidity and mortality both in a UK context and internationally. This study identifies important differences in the risk of adverse outcomes by maternal age, which align with the United Nations sustainable development goals [33] and the targets outlined in the Every Woman, Every Child Global Strategy.[34] Pre-term births and low birth weights are a major cause of neonatal death and cause more than 1 million deaths globally per year.[35] In addition to this the second leading cause of death for young women aged 15-19 years is complications during pregnancy and childbirth.[36] Identifying characteristics which put individuals at higher risk of these complications will help in targeting interventions to populations which are appropriate to their setting.

A significant strength of this study is that it utilises a large cohort study meaning that the majority of statistical analyses do not suffer from problems due to small numbers and the population recruited the cohort is largely representative of the population as a whole. There are however some small difference between the populations recruited and not recruited which should be acknowledged. A lower proportion of mothers aged 20-24 years were recruited compared to those not in the cohort and a higher proportion of South Asian and primiparous women. A lower proportion of mothers at the lower end of the control group may therefore have had some bearing on the prevalence of some outcomes in that group, which is a limitation of this study.

Attempts were made to control for the effect of confounding variables in the multivariate logistic regression model by including a measure of socio-economic deprivation and ethnicity in the model and by restricting the analysis to primiparous women delivering a singleton. These variables were selected due to their

independent association with the outcome variables. Other variables were not included in the model due to a high degree of correlation between variables. There still exists however the possibility that the effect sizes detected in this study are influenced by unmeasured or residual confounding variables.

Despite the large numbers overall there was still only a relatively small number of adolescent women in the cohort, particularly in the sub-group analysis. Stillbirth, premature deliveries and very and extremely low birthweights were also relatively rare events meaning that this study may have failed to detect differences in outcomes between groups due to being insufficiently powered.

The availability of routine hospital data linked to the cohort data was also a significant strength of this study. The use of this data did however also present limitations in that the analysis was restricted to the variables collected routinely and there was no opportunity to recover missing data.

CONCLUSIONS

This study identifies some important variations in obstetric and perinatal outcomes by maternal age. Extremely low birth weight and extremely pre-term delivery were concerns for adolescent mothers. Findings relating to maternal outcomes were also consistent with the existing literature showing lower risk of gestational diabetes, caesarean delivery and instrumental birth. Further work to establish the causal mechanisms behind the links between maternal age and maternal and neonatal outcomes would be advantageous, particularly for adolescent mothers where there are significant gaps in the existing literature.

Figure 1.Details of the Born in Bradford cohort and sub-set used for the present study

Shows participants recruited to the main Born in Bradford cohort study and the sub-set of these participants whose data is used in the present study.

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COMPETING INTERESTS

The authors declare that they have no competing interests

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AUTHOR'S CONTRIBUTIONS

Katie Marvin-Dowle: Completion of data analysis and responsible for writing the manuscript.

Karen Kilner: Providing specialist input on statistical methods

Victoria Burley: Providing specialist input on methods and structure, providing comments and making amendments to the manuscript.

Hora Soltani: Providing specialist input on methods and structure, providing comments and making amendments to the manuscript.

ACCESS TO DATA

Requests for access to data should be addressed to the corresponding author or to the Born in Bradford programme manager rosie.mceachan@bthft.nhs.uk

REFERENCES

[1] Cook SMC, Cameron ST. Social issues of teenage pregnancy. *Obstetrics, Gynaecology & Reproductive Medicine*. 2015; 25(9):243-8
[2] Ganchimeg T, Ota E, Morisaki N, et.al Pregnancy and childbirth outcomes among adolescent mothers: a World Health Organization multicountry study. *BJOG: An International Journal of Obstetrics & Gynaecology*. 2014 Mar 1;121(s1):40-8.
[3] Gilbert WM. Jandial D. Field NT. Birth outcomes in teenage pregnancies. *J Matern Fetal Neonatal Med*. 2004;16(5):265-270.
[4] Tyrberg RB, Blomberg M, Kjolhede P. Deliveries among teenage women - with emphasis on incidence and mode of delivery: A swedish national survey from 1973 to 2010. *BMC Pregnancy Childbirth*. 2013; 9;13(1):1

[5] Mohsin M, Bauman A, Jalaludin B. The influence of antenatal and maternal factors on stillbirths and neonatal deaths in New South Wales, Australia. *J Biosoc Sci.* 2006; 38(05):643-57
[6] Blomberg M. Tyrberg RB. Kjolhede P. Impact of maternal age on obstetric and neonatal outcome with emphasis on primiparous adolescents and older women: A swedish medical birth register study. *BMJ Open*. 2014;4(11):e005840.
[7] Gibbs CM, Wendt A, Peters S, et.al The impact of early age at first childbirth on maternal and infant health. *Paediatr Perinat Epidemiol*. 2012;26:259-284.
[8] Kenny, L. C., Lavender, T., McNamee, R., et.al. Advanced maternal age and adverse pregnancy outcome: evidence from a large contemporary cohort, 2013; 8(2):e56583
[9] Pollack, H., Lantz, P. M., Frohna, J. G. Maternal smoking and adverse birth outcomes among singletons and twins. *American Journal of Public Health*, 2000;90(3), 395.
[10] Jaddoe, V. W., Bakker, R., Hofman, A., Mackenbach, J. P., Moll, H. A., Steegers, E. A., & Witteman, J. C. Moderate alcohol consumption during pregnancy and the risk of low birth weight and preterm birth. The generation R study. *Ann Epidemiol*, 2007; 17(10), 834-840.
[11] Blumenshine, P., Egerter, S., Barclay, C. J.,et.al A. Socioeconomic disparities in adverse birth outcomes: a systematic review. *Am J Prev Med*, 2010;*39*(3), 263-272.
[12] East, P. L., & Felice, M. E. Adolescent pregnancy and parenting: Findings from a racially diverse sample. Psychology Press.2014
[13] Wright, J., Small, N., Raynor, P., et.al Cohort profile: the Born in Bradford multi-ethnic family cohort study. *Int J Epidemiol*,2013; 42(4), 978-991.
[14] West, J., Lawlor, D. A., Fairley, L., Wright, J.. Differences in socioeconomic position, lifestyle and health-related pregnancy characteristics between Pakistani and White British women in the Born in Bradford prospective cohort study: the influence of the woman's, her partner's and their parents' place of birth. *BMJ open*, 2014;4(6), e004805.
[15] Fairley, L., Petherick, E. S., Howe, L. D., et.al. Describing differences in weight and length growth trajectories between white and Pakistani infants in the UK: analysis of the Born in Bradford birth cohort study using multilevel linear spline models.*Archives of disease in childhood*, 2013; archdischild-2012.
[16] Gardosi J, Chang A, Kalyan B, Sahota D, Symonds EM. Customised antenatal growth charts. The Lancet. 1992 Feb 1;339(8788):283-7.
[17] Office for National Statistics, English indices of deprivation 2015, [online] accessed 17.11.17 available from https://www.gov.uk/government/statistics/english-indices-of-deprivation-2015
[18] Saugstad, O. D., Aune, D. Optimal oxygenation of extremely low birth weight infants: a meta-analysis and systematic review of the oxygen saturation target studies. *Neonatology*, 2013;*105*(1), 55-63.
[19] Dos Santos, E. S. L., De Kieviet, J. F., Königs, M., et.al. Predictive value of the Bayley scales of infant development on development of very preterm/very low birth weight children: a meta-analysis. *Early Hum. Dev.*, 2013;*89*(7), 487-496.
[20] Goldenberg RL, Culhane JF, Iams JD, Romero R. Epidemiology and causes of preterm birth. *The Lancet*. 2008 Jan 11;371(9606):75-84.
[21] Goldenberg RL, Culhane JF, Iams JD, Romero R. Epidemiology and causes of preterm birth. The lancet. 2008 Jan 11;371(9606):75-84.
[22] Valsamakis G, KANAKA-GANTENBEIN CH, MALAMITSI-PUCHNER AR, Mastorakos G. Causes of intrauterine growth restriction and the postnatal development of the metabolic syndrome. Annals of the New York Academy of Sciences. 2006 Dec 1;1092(1):138-47.
[23] Horta BL, Victora CG, Menezes AM, Halpern R, Barros FC. Low birthweight, preterm births and intrauterine growth retardation in relation to maternal smoking. Paediatric and perinatal epidemiology. 1997 Apr 1;11(2):140-51.

[24] Nordentoft M, Lou HC, Hansen D, Nim J, Pryds O, Rubin P, Hemmingsen R. Intrauterine growth retardation and premature delivery: the influence of maternal smoking and psychosocial factors. American journal of public health. 1996 Mar;86(3):347-54.

[25] Tommy's, *Premature Birth Statistics,* [online] accessed 17.11.17 available from https://www.tommys.org/our-organisation/why-we-exist/premature-birth-statistics

[26] Van Ham, M. A., Van Dongen, P. W., Mulder, J. Maternal consequences of caesarean section. A retrospective study of intra-operative and postoperative maternal complications of caesarean section during a 10-year period. *European Journal of Obstetrics & Gynecology and Reproductive Biology*, 1997;*74*(1), 1-6.

[27] Lydon-Rochelle, M., Holt, V. L., Martin, D. P.,et.al. Association between method of delivery and maternal rehospitalization.*Jama*, 2000;*283*(18), 2411-2416.
[28] Jolly, M., Sebire, N., Harris, J., et.al The risks associated with pregnancy in women aged 35 years or older. *Hum. Reprod.*,2000; 15(11), 2433-2437.
[29] Jacobsson, B., Ladfors, L., Milsom, I. Advanced maternal age and adverse perinatal outcome. *Obstet Gynecol*, 2004;*104*(4), 727-733.
[30] Freinkel, N., Metzger, B. E., Phelps, R. L., Gestational diabetes mellitus: heterogeneity of maternal age, weight, insulin secretion, HLA antigens, and islet cell antibodies and the impact of maternal metabolism on pancreatic B-cell and somatic development in the offspring. *Diabetes*, 1985;*34*(Supplement 2), 1-7.
[31] Khashan AS, Baker PN, Kenny LC. Preterm birth and reduced birthweight in first and second teenage pregnancies: a register-based cohort study. *BMC pregnancy and childbirth*. 2010 Jul 9;10(1):36.
[32] De Vienne CM, Creveuil C, Dreyfus M. Does young maternal age increase the risk of adverse obstetric, fetal and neonatal outcomes: a cohort study. *European Journal of Obstetrics & Gynecology and Reproductive Biology*. 2009 Dec 31;147(2):151-6.
[33] Public Health England, Teenage Parent Outcomes Modelling Tool, available from http://www.chimat.org.uk/teenconceptions/chimattools, date accessed 12.12.16

[34] United Nations, Sustainable Development Goals, available from http://www.undp.org/content/undp/en/home/sustainable-development-goals.html, date accessed 12.12.16

[35] Child EW. Global Strategy for Women's, Children's and Adolescents' Health. New York, NY: Every Woman Every Child. 2015.

[36] World Health Organisation, Adolescent Pregnancy Fact Sheet, available from http://www.who.int/mediacentre/factsheets/fs364/en/ , accessed 12.12.16

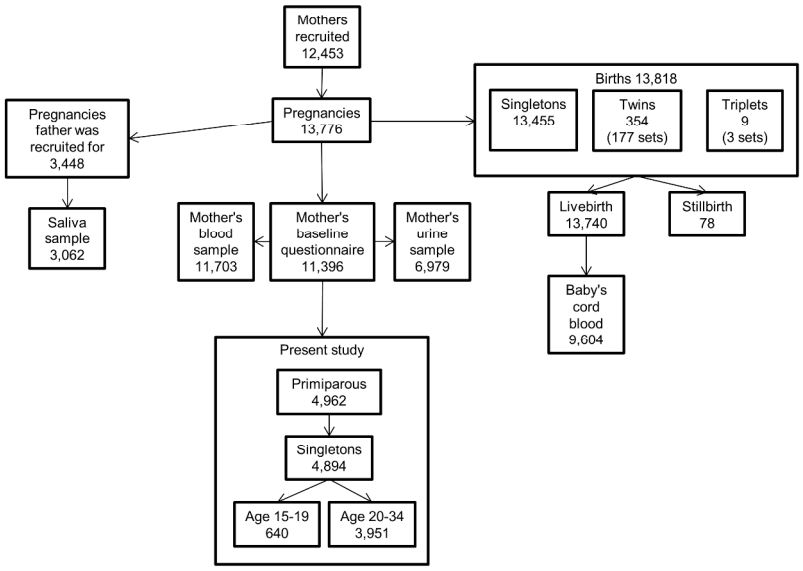

Figure 1.Details of the Born in Bradford cohort and sub-set used for the present study

254x190mm (300 x 300 DPI)

STROBE Statement—Checklist of items that should be included in reports of ***cohort studies***

	Item No	Recommendation	Page No.
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	2
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3-5
Objectives	3	State specific objectives, including any pre-specified hypotheses	5
Methods			
Study design	4	Present key elements of study design early in the paper	5-7
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5-6
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	5-6
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed	NA
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6-8
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	6-7
Bias	9	Describe any efforts to address potential sources of bias	8
Study size	10	Explain how the study size was arrived at	6
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	6-8
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	7-8
		(*b*) Describe any methods used to examine subgroups and interactions	8
		(*c*) Explain how missing data were addressed	8
		(*d*) If applicable, explain how loss to follow-up was addressed	NA
		(*e*) Describe any sensitivity analyses	NA
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	11-12, 14, 17,19
		(b) Give reasons for non-participation at each stage	NA
		(c) Consider use of a flow diagram	6
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	11-12
		(b) Indicate number of participants with missing data for each variable of interest	11-12, 14
		(c) Summarise follow-up time (eg, average and total amount)	NA

Outcome data	15*	Report numbers of outcome events or summary measures over time	14, 17,19
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	17,19
		(*b*) Report category boundaries when continuous variables were categorized	6-8
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	NA
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	18-19
Discussion			
Key results	18	Summarise key results with reference to study objectives	20-21
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	23-24
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	22-24
Generalisability	21	Discuss the generalisability (external validity) of the study results	22
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	25

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.